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Application of the NMR Method in the Study of Simple and Complex Hydrides of Light Metals

G.N.Boiko, Yu.I.Malov, and K.N.Semenenko

The review discusses the results of studies on simple and complex hydrides of light metals by NMR, in particular the relation between the parameters of the NMR spectra and molecular structure, the formation of complexes by the hydrides and the stability of such complexes, as well as the characteristic features of the spectra of hydroborate systems.
The bibliography includes 101 references

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I. INTRODUCTION

The results of studies on simple and complex hydrides, in particular boron and aluminium hydrides, by the NMR method are discussed in the present review. In all the tables quoted the spin–spin coupling constants J are expressed in hertz units (Hz), the chemical shifts are given in parts per million (p.p.m.), the δH are relative to $Si(CH_3)_4$, and the $\delta^{11}B$ are relative to $BF_3.(C_2H_5)_2O$. To facilitate comparison, data obtained by different investigators relative to other standards have been recalculated relative to the standards quoted above in accordance with the formulae quoted in the literature[1-10]. The minus sign of δ corresponds to a shift of the signals to low fields relative to the standard. The discrepancies between the chemical shifts found by different workers are most probably due to the use of different solvents (see, for example, Refs. 11–13).

II. COMPOUNDS CONTAINING PYRAMIDAL GROUPS

1. Complexes of the Type $BH_3.L$

Table 1 presents the literature values of the chemical shifts and the constants J_{B-H} for borane complexes with different ligands containing electron donating atoms of Group V and VI elements (O, S, N, and P).

These results make it possible to infer the following changes in the NMR spectra of the donor and acceptor molecules on complex formation.

1. The resonance signals due to the nuclei of the electron-accepting molecules are as a rule displaced towards higher fields relative to the chemical shifts due to the same nuclei in the molecules of the free components. On the other hand, the signals due to the nuclei of the electron-donating molecules shift towards lower

fields. The increase of the shielding of the boron atom on formation of complexes of the type $BH_3.L$ can be explained by a decrease of the paramagnetic contribution to the shielding through the transfer of electrons from the donor to the unfilled p_z boron orbital and the change in the hybridisation of boron from sp^2 to sp^3. This is confirmed also by the value of the spin–spin coupling constant J_{B-H}. It has been shown[7,16] that the J_{B-H} increases from 81 to 136 Hz when boron passes from the sp^2- to the sp^3-state. For the complexes $BH_3.L$, J_{B-H} is in the range 90–106 Hz. On this basis, it was concluded[7,16] that the B–H bonds in the complexes are in a state of hybridisation intermediate between sp^2 and sp^3.

Table 1. The NMR parameters of borane complexes.

Compound	δ^{11} B	J_{B-H}	δ BH_3	δ CH_3	δ CH_2	$\delta CH_3 - \delta CH_2$	References
1	2	3	4	5	6	7	8
$(CH_3)_2O \cdot BH_3$	−2.5	104	—	−3.71	—	—	14,15
$(CH_3)_4O \cdot BH_3$	0.9	103	—		−4.00	—	8,14,15,16
$(C_2H_5)_2O \cdot BH_3$		134			−2.11	2.28	14
$(C_2H_5)_2O \cdot BHCl_2$	6	130	—	−1.28	−1.95	0.67	17
$(C_2H_5)_2O \cdot BCl_3$				−1.60	−4.84	3.24	14,18,19
$(CH_3)_2S \cdot BH_3$	20.1	—	—	—	—	—	15
$(CH_3)_4S \cdot BH_3$	20.1	—	—	—	—	—	15
$(CH_3)_3N \cdot BH_3$	8.1	96–98	−1.62	−2.58	—	—	15,16,20–26
$(CH_3)_2NH \cdot BH_3$	14.5	94–96	−1.46	−2.52	—	—	16,21,25,26
$CH_3NH_2 \cdot BH_3$	18.5	93–96	−1.32	−2.55	—	—	21,25,26
$NH_3 \cdot BH_3$	23.1	91–94	−1.29	—	—	—	21,26
$(C_2H_5)_3N \cdot BH_3$	13.4	—	−1.38	−1.13	−2.75	1.62	8,21,22
$(C_2H_5)_3N \cdot BH_2Cl$	1.7	—	—	—	—	—	27
$(C_2H_5)_3N \cdot BCl_3$	9.7	—	—	—	—	—	28
$(C_2H_5)_3N \cdot BH_2Br$	6.7	—	—	—	—	—	27
$(C_2H_5)_3N \cdot BBr_3$	5.4	—	—	—	—	—	8,28
$(C_2H_5)_3N \cdot BH_2I$	16.7	—	—	—	—	—	27
$(C_2H_5)_3N \cdot BI_3$	60.1	—	—	—	—	—	8,28
$(CH_3)_3P \cdot BH_3$	36.8	103–104	−0.44	−1.24	—	—	15,21,29–31
$(CH_3)_2PH \cdot BH_3$	37.4	90–96	−0.43	—	—	—	8,16,32
$CH_3PH_2 \cdot BH_3$	—	—	−0.53	—	—	—	31,33
$PH_3 \cdot BH_3$	42.5	103–104	−0.53	—	—	—	31,33
$PF_3 \cdot BH_3$	48.3	107	—	—	—	—	31
$PHF_2 \cdot BH_3$	42.1	103	—	—	—	—	31
$[(CH_3)_2N]_3P \cdot BH_3$	43	96	—	−2.63	—	—	29
$[(CH_3)_2N]_3P \cdot BH_2Cl$	21	124	—	−2.72	—	—	29
$[(CH_3)_2N]_3P \cdot BHCl_2$	6	144	—	−2.79	—	—	29
$[(CH_3)_2N]_3P \cdot BCl_3$	3	—	—	−2.84	—	—	29
$(CH_3O)_3P \cdot BH_3$	46	96	−0.33	−3.73	—	—	25,29,34,35
$(CH_3O)_3P \cdot BH_2Br$	30	131	—	−3.84	—	—	29
$(CH_3O)_3P \cdot BHBr_2$	21	142	—	−4.05	—	—	29
$(CH_3O)_3P \cdot BBr_3$	20	—	—	−4.16	—	—	29
$(C_2H_5)_3P \cdot BH_3$	42	96	−0.20	−1.12	−1.60	0.48	17,29
$(C_2H_5)_3P \cdot BH_2Cl$	20	115	—	−1.20	−1.82	0.62	17
$(C_2H_5)_3P \cdot BHCl_2$	6	131	—	−1.28	−1.95	0.67	17
$(C_2H_5)_3P \cdot BCl_3$	3	—	—	−1.32	−2.08	0.76	17
$(C_2H_5)_3P \cdot BH_2Br$	25	111	—	−1.23	−1.86	0.63	17
$(C_2H_5)_3P \cdot BHBr_2$	16	128	—	−1.31	−2.05	0.74	17
$(C_2H_5)_3P \cdot BBr_3$	15	—	—	−1.39	−2.21	0.82	17

2. Changes are observed in the chemical shifts of nuclei not directly involved in the formation of donor–acceptor bonds. These changes are smaller the more remote is the given atom from that involved in the formation of the coordinate bond. One may conclude that the donor–acceptor interaction alters the electronic structure of both donor and acceptor molecules. However, the electron density of the atoms in the α-position relative to those joined by the coordinate bond changes to the greatest extent.

In NMR studies on borane complexes much attention is devoted to the problem of the possible use of ^1H and ^{11}B chemical shifts as characteristics of the relative stabilities of the complexes. For example, the shielding of the boron nuclei in the acceptors and the deshielding of the nuclei forming part of the donor molecules (L) increase in the sequence $BF_3 < BCl_3 < BBr_3 < BI_3$ in the complexes BX_3 (X = halogen) with any ligands L[36–38]. This sequence of electron accepting capacities coincides with the sequence of the enthalpies of formation of boron halide complexes with pyridine[37,38]. It follows from the NMR data that the complex $BH_3.P(CH_3)_3$ is more stable than $BH_3.N(CH_3)_3$. This is explained by a shift[39] of the electrons in the B–H bonds to the 3*d* orbital of phosphorus. The hypothesis of the $d\pi - p\pi$ interaction in complexes with phosphines has not been confirmed. The shift of the electrons localised in the B–H bond should lead to a decrease of the hydrogen atom electron density and hence displace the signal to lower fields. In reality the opposite behaviour is observed in the ^1H spectra of $BH_3.P(CH_3)_3$ and $BH_3.N(CH_3)_3$: the chemical shifts of the protons in the B–H bonds are −0.44 and −1.62 p.p.m. respectively. The sequence of the changes in the NMR parameters is frequently inconsistent with the expectation based on the energy of the donor–acceptor interaction[21,23]. For example, a correlation is observed[21] between the number of methyl groups at the nitrogen atom in the complexes $BH_3.NH_{3-n}(CH_3)_n$ and the ^1H and the ^{11}B chemical shifts. Table 1 shows that, on passing from NH_3 to $N(CH_3)_3$, the signals are monotonically displaced towards lower fields. The change in the proton chemical shifts is evidence for a systematic increase of the *s*-character of the boron orbitals in the direction of hydrogen atoms with increase of the number of methyl groups at the nitrogen atom. The *s*-character of the fourth boron orbital and its capacity for donor–acceptor interaction should decrease in the same sequence. In such a case the ^{11}B chemical shifts should diminish on passing from $BH_3.NH_3$ to $BH_3.N(CH_3)_3$, which does in fact occur. However, this is inconsistent with the finding that borane–amine complexes are more stable than the complexes with ammonia[24].

The change in the electronegativity of the donor and acceptor atoms on complex formation is also indicated by the changes in the internal shifts of the protons of the ethyl groups linked to these atoms. A linear correlation between the electronegativity of X and the internal proton shift, expressed as the difference $\delta CH_3 - \delta CH_2$, has been established[40–43] for $(C_2H_5)_nX$. This correlation is also valid for molecules combined in a complex[22,44–46]. The internal proton shift in compounds of the type $(C_2H_5)_nX$, which behave as donors (X = O, S, N, or P), as a rule increases, while in compounds behaving as acceptors (X = metal) it decreases. Consequently the electronegativity of donor atoms increases on complex formation and that of acceptor atoms diminishes, in agreement with the decrease or increase of electron density at the atom X as a result of charge transfer from the donor to the acceptor. Thus the internal shifts of the protons in the ethyl groups decrease in the complexes $BH_nX_{3-n}.(C_2H_5)_3P$ (X = halogen)[17]. This means that the electron density at the phosphorus atom diminishes on complex formation. The internal shifts give rise to the following sequence of the electron-accepting capacities of boron compounds: $BBr_3 > BCl_3 > BHBr_2 > BHCl_2 > BH_2Br > BH_2Cl > BH_3$.[17] It is significant that this sequence is confirmed by the enthalpies of formation of the BBr_3, BCl_3, and BH_3 complexes with pyridine[37,38]:

Complex	$C_5H_5N \cdot BBr_3$	$C_5H_5N \cdot BCl_3$	$C_5H_5N \cdot BH_3$
$-\Delta H^\circ$ kcal mole^{-1}	32.0	30.8	28.8

Thus the study of the NMR spectra of borane complexes yields information about the nature of the changes in the electronic structures of the components of the complex. Bearing in mind the complexity of the dependence of the chemical shifts on a number of factors, definite $\Delta H^\circ - \delta$ relations can be expected only for series of compounds with similar structures.

2. Complexes of the Type $AlH_3.L$

Table 2 presents data for the proton chemical shifts in several aluminium complexes. Their analysis makes it possible to infer the following changes in the electronic structure of the donor and acceptor molecules on complex formation.

Table 2. The proton chemical shifts in the spectra of coordination compounds of aluminium hydride.

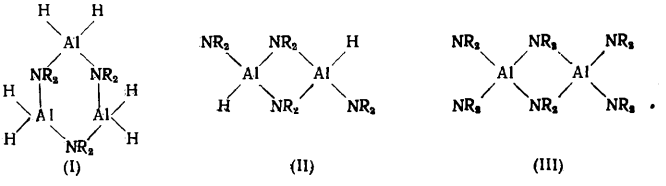
Compound	δ AlH	δ CH_3	δ CH_2	δ CH_2–X	References
$H_3Al\cdot OC_4H_8$	−4.08	−3.81 −1.43	—	—	47
$H_3Al\cdot N(CH_3)_3$	−3.81	—	—	−2.08	47–50
$H_3Al\cdot 2OC_4H_8$	−3.61	−4.13 −2.25	—	—	47
$H_3Al\cdot 2N(CH_3)_3$	−3.56	—	—	−2.25	47
$H_3Al\cdot 2O_2C_4H_8$	−3.56	−4.03	—	—	47
$H_3Al\cdot N(CH_3)_3\cdot OC_4H_8$	−3.56	−4.13 −2.25	—	−2.75	47
$H_3Al\cdot N(CH_3)_3\cdot O_2C_4H_8$	−3.56	−4.13	—	−2.75	47
$H_3Al\cdot OC_4B_8\cdot O_2C_4H_8$	−3.56	−4.1 −2.25	—	—	47
$H_3AlC_2H_5\cdot N(CH_3)_3$	−3.54	0.20	−0.97	−2.48	48
$HAl(C_2H_5)_2\cdot N(CH_3)_3$	—	0.15	−1.09	−2.38	48
$H_2AlCH_3\cdot N(CH_3)_3$	−3.54	—	0.80	−2.46	48
$HAl(CH_3)_2\cdot N(CH_3)_3$	—	—	0.83	−2.39	48
$HAlCl_2\cdot O(CH_3)_2$	−3.1	—	—	−3.9	51
$HAlCl_2\cdot O(C_2H_5)_2$	—	−4.41	—	−1.6	51
$HAlCl_2\cdot OC_4H_8$	−2.1	−3.6 −1.7	—	—	51
$H_3Al\cdot P(C_2H_5)_3$	−3.33	−1.71	−1.15	—	52
$H_2AlCl\cdot P(C_2H_5)_3$	—	−1.78	−1.18	—	52
$HAlCl_2\cdot P(C_2H_5)_3$	—	−1.82	−1.20	—	52
$AlCl_3\cdot P(C_2H_5)_3$	—	−1.96	−1.26	—	52

1. With increase of the coordination number (C.N.) of aluminium or with increase of the electron-donating capacity of the ligand for the same coordination number, the chemical shift of the protons linked directly to aluminium increases. This indicates an increase of electron density at the nuclei of the acceptor molecule, caused by charge transfer from the donor.

2. The NMR data for 1 : 1 and 1 : 2 complexes lead to the conclusion that the strength of the bond between aluminium and the ligand $N(CH_3)_3$ is greater than for OC_4H_8†, since the chemical shift of the hydride protons in $AlH_3.N(CH_3)_3$ is greater than in $AlH_3.OC_4H_8$. On formation of mixed 1 : 2 complexes, differences in the shielding of the H–Al protons are not observed. At the same time an excess of tetrahydrofuran (THF) is necessary for the addition of a second OC_4H_8 molecule to the complex $AlH_3.OC_4H_8$.[47]

3. No changes were observed in the chemical shifts of the protons of the CH_3 groups in the NMR spectra of the complex $AlH_3.N(CH_3)_3$ and therefore the state of the $N(CH_3)$ molecule changes only slightly on coordination. The free electron pair of the nitrogen atom in the $N(CH_3)_3$ molecule is involved in sp^3 hybridisation. If a coordinate bond is formed, there is no change in the valence state of carbon. On the other hand, in the complex $AlH_3.2OC_4H_8$ the proton resonance frequency in the α-CH_2 group decreases by 10 Hz, while the resonance frequency for β-CH_3 protons remains unchanged. This indicates alterations in the valence state of the oxygen atom. The NMR spectra of the complexes $H_{3-n}AlX_n.2OC_4H_8$ (n = 1, 2; X = Cl, Br, or I) indicate descreening of the protons in the α- and β-CH_2 groups in THF due to electron withdrawal from the oxygen atom to the aluminium atom[53]. The internal shift of the ethyl protons in the compounds $AlH_nCl_{3-n}.P(C_2H_5)_3$ increases[52] with increase of the degree of substitution of hydrogen atoms by chlorine. This change in the internal shift indicates an increase in electron-accepting capacity in the sequence $AlCl_3 > AlCl_2H > AlClH_2 > AlH_3$. Unfortunately the enthalpies of formation of these complexes are not available, which precludes their comparison with NMR data.

The structures of the above complexes in solution can change markedly as a result of association. The degree of association becomes more marked on passing to complexes with higher dipole moments and also on formation of hydrogen bond bridges of the type Al–H–Al or Al–H_2–Al. The existence of hydrogen bond bridges should have been reflected in the corresponding ^1H NMR shifts or should have given rise to additional signals. For complexes of aluminium hydride with trimethylamine, THF, and dioxane, not more than one signal due to the proton linked directly to the aluminium nucleus was observed[47]. The $R_2AlH.N(CH_3)_3$ and $RAlH_2.N(CH_3)_3$ complexes can undergo a different type of association via the methyl group for R = CH_3 and via the methylene group for R = C_2H_5. This follows from the splitting of the lines in the ^1H NMR spectra of these compounds in cyclohexane[48]. Moreover the formation of the dimer $Al_2(C_2H_5)_6$ does in fact proceed via the CH_3 group, which has also been confirmed by NMR. The ^1H NMR spectra of amino-aluminium hydrides of the type $H_{3-n}Al(NR_2)_n$ (n = 1, 2, or 3; R = CH_3 or C_2H_5) have been investigated[54]. It was shown that in benzene solutions association takes place via the formation of Al–N–Al linkages and the most probable structures (I)–(III) were proposed:



(I) (II) (III)

The formation of bridged structures is confirmed by the presence in the ^1H NMR spectra of two signals due to NR_2 with both R = CH_3 and R = C_2H_5. Infrared spectroscopic data are consistent with those derived from ^1H NMR.[54] The association of complexes of the type $AlF_nCl_{3-n}.THF$ (n = 1 or 2) proceeds via the fluorine atoms[55].

Thus the chemical shifts and the spin–spin coupling constants yield information about the changes in the distribution of electron density, about the capacity for hybridisation, and about the amount of ionic character of the bonds when the molecules are bound in a complex.

III. COMPOUNDS CONTAINING TETRAHEDRAL GROUPS

Table 3 presents the ^{11}B NMR parameters for certain ionic hydroborates.

The ^1H NMR spectrum of an aqueous solution of $NaBH_4$ contains a quartet with the relative intensities 1 : 1 : 1 : 1 and a weak septet[58–61]. In the ^{11}B NMR spectrum there is a 1 : 4 : 6 : 4 : 1 quintet. The fine structure of the spectrum was determined using double resonance. On irradiation of the boron nucleus, the initial quartet is converted into a single line. This indicates the equivalence of all the protons in the BH_4^- anion and their interaction with ^{11}B.

† OC_4H_8 = THF.

Such equivalence is possible if the tetrahydroborate ion has a square planar, pyramidal, or tetrahedral structure. The first two models should lead to relatively more marked variation of the electric field gradients at the boron atom with the angle and this should be reflected in a broadening of the ^1H NMR lines. Narrow lines in the quartet are observed experimentally, which implies that the tetrahydroborate ion is most likely to have the tetrahedral structure. The boron chemical shifts for $LiBH_4$ depend, according to Ehemann et al.,[57] on the concentration of the solution and the type of solvent, i.e. apparently on the degree of separation of the cation and anion due to solvation effects.

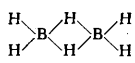
Table 3. The ^{11}B NMR parameters of certain ionic tetrahydroborates.

Compound	Solvent	$\delta^{11}B$	J_{B-H}	References
$NaBH_4$	0.1 *N* NaOH	43.8	81	16
$LiBH_4$	Ether	38.2	75	56
$[(C_4H_9)_4N]BH_4$	THF	37.7	82	57
$[(C_{18}H_{17})NC_3H_7]BH_4$	Benzene	36.9	82	57

IV. COVALENT HYDROBORATES WITH BRIDGE BONDS

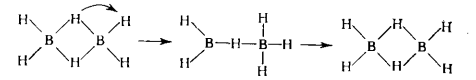
1. Diborane and Its Derivatives

It has been established by electron diffraction[62] and infrared spectroscopy[63,64] that the electron-deficient diborane molecule has a bridged structure:

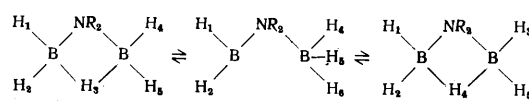


In this structure four hydrogen atoms are linked directly to the boron atoms by the usual covalent two-electron bonds, while the remaining two hydrogen atoms occupy bridging positions, saturating the remaining valences of the boron atoms. The ^1H and ^{11}B NMR spectra of liquid diborane are consistent with the bridged model[32,37,61,64-67]. Thus the ^{11}B NMR spectrum at $f = 30$ MHz contains one multiplet consisting of a triplet of triplets[32]. The major triplet splitting arises in consequence of the spin–spin interaction of the boron nuclei with the two equivalent terminal protons and the minor splitting is due to the interaction of the boron atom with the pair of bridge hydrogen atoms. An additional confirmation of the bridged structure of B_2H_6 is provided by its ^1H NMR spectrum, from which the existence of two different types of protons follows directly. At a frequency of 30 MHz the ^1H NMR spectrum consists of a complex multiplet. The interpretation of this spectrum shows to a first approximation that the observed component lines have the following origins: a quartet corresponds to the terminal hydrogen atoms linked to one ^{11}B atom ($I = 3/2$) while a septet corresponds to the bridge hydrogen nuclei linked to the two boron nuclei. When the interaction with the boron nuclei is suppressed by double resonance, the two different types of protons are represented in the ^1H NMR spectrum by two singlets with the area ratio 2 : 1. The signals due to the hydrogen nuclei linked to ^{10}B ($I = 3$) form a weak septet. The bridge protons resonate in a higher field than the terminal protons. This shows that the B–H–B linkage is more ionic than B–H. This is also indicated by the ratio of the spin coupling constants. Overall, the NMR parameters show that the electron cloud density at the bridge protons is higher than at the terminal protons. The results of a quantum-mechanical calculation of the magnetic shielding of protons in diborane are consistent with this conclusion[68]. Subsequently the NMR spectra of liquid diborane were investigated on spectrometers with a higher working frequency and with a higher resolving power[66,67]. With increase of the working frequency, the centres of the multiplets are separated and the interpretation of the spectrum is simplified. In addition, the increase in the resolving power of the apparatus made it possible to observe more remote spin–spin interactions of the nuclei in the diborane molecule. According to modern ideas, the spin system of B_2H_6 belongs to the type $A_2A'_2M_2XX'$, in which the two boron nuclei (X and X′) are magnetically nonequivalent owing to the different degrees of spin–spin interaction with the terminal protons (A_2, A'_2).

There are solvents in which the terminal and bridge protons appear to be magnetically equivalent, for example the spectrum of diborane in ethyl ether at −26°C consists of a triplet of triplets, the structure of the spectrum changes with increase of temperature, and at 84°C a septet is observed[69]. In the ^{11}B NMR spectrum of diborane in the dimethyl ether of ethylene glycol a septet is observed at room temperature. The authors explain the equivalence of the protons by rapid intramolecular exchange via the following scheme:



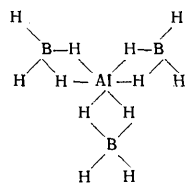
In this scheme the unstable intermediate species may be stabilised by interaction with a solvent molecule, which behaves as an electron donor. The ^{11}B NMR spectra of the products of the reactions of diborane with inorganic and organic anions indicate the formation of substituted hydroborate anions[70-73]. According to Geines and Schaeffer[26], the chemical shifts of the boron nuclei in the aminodiboranes $B_2H_5NH_2$, $B_2H_5NHCH_3$, and $B_2H_5N(CH_3)_2$ are respectively 26.7, 22.7, and 17.0 p.p.m., i.e. the signals shift towards lower fields with increase of the number of methyl groups at the nitrogen atom. Phillips et al.[16] observed that, on raising the temperature from −10° to 40°C, the ^{11}B resonance lines in the $B_2H_5N(CH_3)_2$ spectrum are broadened and the splitting into doublets almost vanishes. The authors explained the breakdown of the spin–spin interaction of boron with the bridge protons by partial dissociation of the B–H–B linkage with subsequent rotation of the BH_3 group about the B–N bond and the formation of a new B–H–B linkage involving a different hydrogen atom. As a result, all the protons become equivalent:



Williams et al.[74] investigated the ^{11}B NMR spectra of various methyldiboranes and their deuterio-derivatives. Their results show that the replacement of hydrogen by a methyl group shifts the ^{11}B signal to a lower field. A more detailed analysis of the ^1H NMR spectra of these compounds is described in the literature[75-77].

2. Aluminium Tetrahydroborate

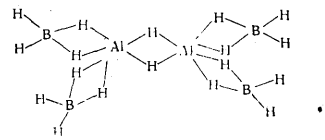
In the aluminium tetrahydroborate structure, proposed on the basis of electron diffraction studies[78] and infrared spectra[79], the aluminium atom is located at the centre of an equilateral triangle formed by the boron atoms. Four hydrogen atoms are linked to each boron atom, so that the latter is in a tetrahedral environment. Two of these hydrogen atoms form bridges between the boron atoms and aluminium, i.e. there are two types of protons in the molecule (bridge and terminal protons):



The ^1H and ^{11}B NMR spectra of aluminium tetrahydroborate were first examined by Ogg and Ray[80]. The ^1H NMR spectrum at a frequency of 30 MHz consists of an unresolved multiplet with a line half-width of about 300 Hz. The spectrum was interpreted using the double resonance of aluminium and boron nuclei. On irradiation of the boron nucleus, the resonance line in the proton spectrum becomes somewhat narrower, although it still remains fairly broad (220 Hz). Irradiation of the aluminium nucleus leads to the appearance in the spectrum of a quartet with a splitting of 87 Hz, as for the BH_4^- ion. The ^{11}B NMR spectrum shows a quintet with the intensity ratios 1 : 4 : 6 : 4 : 1, the splitting and positions of which are characteristic of the BH_4^- ions. In the ^{27}Al NMR spectrum there is an unresolved multiplet due to the spin–spin interaction of the aluminium nucleus with the twelve equivalent protons[81]. Interpretation of the NMR spectra of aluminium tetrahydroborate leads to the following conclusions concerning its structure in the liquid phase. Firstly, all the hydride protons in the molecule have the same electronic environment, i.e. they are "chemically equivalent". Secondly, all the protons are linked to both boron and aluminium. The initial broad line in the proton spectrum can be interpreted as a multiplet consisting of 24 lines due to the spin–spin coupling with boron ($I = 3/2$) and aluminium ($I = 5/2$), the components of the multiplets being appreciably broadened owing to the quadrupole relaxation of the aluminium nucleus. Thirdly, each boron nucleus is linked to four equivalent protons. The narrow lines in the ^{11}B NMR quintet indicate a nearly tetrahedral disposition of the protons around the boron atom. These conclusions do not lead to an unambiguous confirmation of the bridged model of aluminium tetrahydroborate proposed on the basis of infrared spectroscopic and electron diffraction studies. The ^1H NMR spectrum of this structure should contain signals due to two types of protons, while in reality all the protons give rise to one common signal. This apparent contradiction can be eliminated by assuming that there is a dynamic process leading to the exchange and averaging of the bridge and terminal protons over a period of time. To elucidate the mechanism of proton exchange in $Al(BH_4)_3$, Ogg and Ray[80] studied the NMR spectra of liquid specimens at temperatures ranging from −40 to 60°C. The spectra of deuterio-derivatives of aluminium tetrahydroborate were investigated and it was shown that the form of the proton spectrum hardly changes with temperature. Deuteriation leads to a broadening of the quartet components in the ^1H NMR spectrum obtained on single irradiation of the aluminium nucleus. These results led the authors to the conclusion that the proton exchange in aluminium tetrahydroborate is non-classical (there is a tunnel effect)[80]. The same investigators showed that at 80°C $Al(BH_4)_3$ undergoes reversible dissociation:

$$2Al(BH_4)_3 \rightleftharpoons Al_2B_4H_{12} + B_2H_6 .$$

A dimeric structure was proposed for $Al_2B_4H_{12}$:



The ^1H NMR spectrum of $Al_2B_4H_{12}$ contains a quartet, in contrast to the broad signal of $Al(BH_4)_3$. It was suggested that the fine structure of the spectrum is due to the rapid rotation of the BH_4 groups, which interferes with the spin–spin interaction between the protons and the aluminium nucleus. The broad signal in the ^1H NMR spectrum of $Al(BH_4)_3$ is converted into a quartet when the temperature of the liquid specimen is raised from −40 to 90°C; this change can be both reversible and irreversible[81]. The authors attribute the observed changes to exchange between two possible structural models of the $Al(BH_4)_3$ molecule—prismatic and octahedral. However, in order to confirm this conclusion, it is necessary to study the kinetics of the transition from one form to the other and also each of these forms in the solid phase.

Table 4. The ^1H and ^{11}B NMR parameters of certain covalent metal tetrahydroborates.

Compound	δ ^{11}B	δ H	J_{B-H}	References
$Mg(BH_4)_2$	42.8	—	83.5	57
$Al(BH_4)_3$	37	−1.50	86	83,84
$Be(BH_4)_2$	34.6	—	84.2	57
$CuBH_4 \cdot P(C_6H_5)_3$	30	—	84	
$Ti(BH_4)_3 \cdot O(C_2H_5)_2$	23	—	—	57
$Hf(BH_4)_4$	14.2	−2.85	90	85,86
$Zr(BH_4)_4$	11.0	−1.58	90	85,86
$Th(BH_4)_4$	8.0	—	86.6	57
B_2H_6	−17.5	−3.92 0.56	135 46	76
$UBH_4(C_5H_5)_3$	−64.0	−74.23	86	87

Williams[82] notes that the occurrence of internal exchange is characteristic not only of aluminium tetrahydroborate but also of many other boron hydrides and their complexes with Lewis bases. The observed equivalence of the protons has been explained by a tautomeric transition in the liquid phase between structures with one and two bridge bonds via hydrogen atoms[82]:

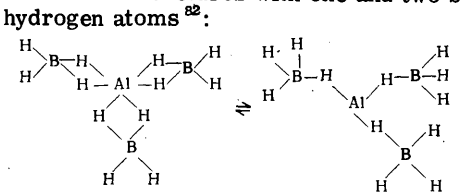


Table 4 presents the results of studies on certain covalent metal tetrahydroborates by NMR.

The observed differences between the ^1H and ^{11}B chemical shifts can probably be explained by differences between the electronic structures of the central atoms. However, the NMR spectra of all these compounds indicate the equivalence of the protons. The disappearance of the fine structure from the ^1H NMR spectrum of $Zr(BH_4)_4$, observed when the temperature is reduced, was explained[88] by the retardation of the intramolecular exchange. However, even at the lowest temperatures it was impossible to ensure the localisation of protons. It has been shown[89] that the observed temperature variation of the spectra of zirconium and hafnium tetrahydroborates is due to the influence of the quadrupole relaxation of the boron nuclei on the resonance of the protons linked directly to these atoms. On the whole, one may say that the studies on covalent tetrahydroborates with bridge bonds by NMR make it possible to draw inferences concerning the bond between the BH_4 group and the central atom and also concerning the mobility of the protons. Diborane is apparently the only example of compounds of this class whose ^1H NMR spectrum shows separate signals due to bridge and terminal protons.

V. COVALENT TETRAHYDROBORATES CONTAINING AN M–L COORDINATE BOND

Table 5 presents the NMR parameters for the $Al(BH_4)_3$ complexes with $N(CH_3)_3$, $P(CH_3)_3$, $As(CH_3)_3$, $O(CH_3)_2$, $S(CH_3)_2$, and $O(C_2H_5)_2$ as well as complexes with hydride derivatives of $Al(BH_4)_3$. The ^{11}B NMR spectra of all these compounds contain a quintet, showing that four identical protons are linked to each boron atom and that all the boron atoms are equivalent in derivatives containing two or more tetrahydroborate groups[84,90]. The presence of four identical protons linked to boron limits the number of possible structures involving the B–N and Al–N–B bridge bonds. The ^1H NMR spectrum of the tetrahydroborate group consists of a broad unresolved signal without the expected fine structure due to the spin–spin interaction of protons with boron and aluminium. However, significant differences between the hydride proton absorption line forms are observed for some of the compounds. For example, the ^1H NMR spectra of the tetrahydroborate group in the complexes with $As(CH_3)_3$ and $S(CH_3)_2$ are split into four lines owing to the spin–spin interaction with boron, while interaction with aluminium is not observed[84]. It has been noted that the proton spectrum of the complex $Al(BH_4)_3.N(CH_3)_3$ contains a multiplet comprising twelve lines, due to the interaction of the protons with boron and aluminium and $J_{B\text{-}H} \simeq 2J_{Al\text{-}H}$.[83,84] There is splitting also in the ^{27}Al NMR spectrum of this compound. The observed differences between the proton spectra of the above compounds can probably be accounted for by the effect of the quadrupole relaxation of the aluminium nucleus. Evidently the electric field gradient at the ^{27}Al nucleus in the complex with $N(CH_3)_3$ is smaller and the rate of relaxation of this nucleus in the compounds with $As(CH_3)_3$ and $S(CH_3)_2$ is much higher than in all the other complexes examined. Thus, using the available information about the absorption line form in the NMR spectra, complexes of the type $Al(BH_4)_3.L$ can be arranged in the following sequence in terms of increasing asymmetry of the electronic environment of the aluminium nucleus:

$$N(CH_3)_3 < P(CH_3)_3 < As(CH_3)_3$$
$$O(CH_3)_2 < S(CH_3)_2$$

At elevated temperatures the signal due to amino-group protons in the ^1H NMR spectrum of $Al(BH_4)_3.N(CH_3)_3$ is split[92], which is associated either with a marked orientation of the ligand in the complex or with the existence of the equilibrium:

$$2Al(BH_4)_3 \cdot N(CH_3)_3 \rightleftharpoons Al(BH_4)_3 \cdot 2N(CH_3)_3 + Al(BH_4)_3 .$$

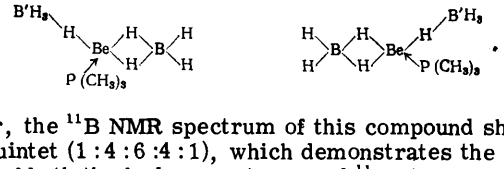
If it is assumed that there is an equilibrium between the 1 : 1 and 1 : 2 complexes, the singlet at −60°C can be attributed to the undissociated form and the two signals at 60°C to the existence of two equilibrium forms of the complex. With decrease of temperature, the components of the multiplet due to the tetrahydroborate protons are broadened, which has been explained[88] by the retardation of proton exchange. However, such spectral changes can be attributed also to the influence of the quadrupole NMR relaxation of boron and aluminium.

Table 5. The ^1H and ^{11}B NMR parameters of aluminium tetrahydroborate complexes.

Compound	^{11}B NMR		^1H NMR				References
	δ ^{11}B	J_{B-H}	δ BH_4	δ CH_3	δ CH_2	J_{B-H}	
$Al(BH_4)_3 \cdot P(CH_3)_3$	35.5	87	−0.63	−0.93	—	87	84
$Al(BH_4)_3 \cdot As(CH_3)_3$	35.6	88	−0.91	−0.97	—	87	84
$Al(BH_4)_3 \cdot O(CH_3)_2$	—	—	−0.70	−3.23	—	—	84
$Al(BH_4)_3 \cdot S(CH_3)_2$	—	—	−0.77	−1.85	—	—	84
$Al(BH_4)_3 \cdot O(C_2H_5)_2$	35.7	85	−0.48	−1.23	−3.15	—	84
$Al(BH_4)_3 \cdot N(CH_3)_3$	37.8	88	−0.73	−0.64		87	81,84
$Al(BH_4)_2H \cdot N(CH_3)_3$	38.2	85	—	—	—	—	90
$AlH_2BH_4 \cdot N(CH_3)_3$	38.4	85	—	—	—	—	90
$Al(C_2H_5)_2BH_4 \cdot N(CH_3)_3$	39.4	85	0.08	−2.40 0.91	— 0.10	84	91

Among complexes of aluminium tetrahydroborate with ammonia, a study has been made on the compound with the empirical formula $Al(BH_4)_3.6NH_3$. The ^1H NMR spectrum in ammonia shows[93] a single quartet characteristic of BH_4^-. This spectrum probably agrees best with the ionic structure $[Al(NH_3)_6^{3+}](BH_4)_3^-$. However, the study of ^{11}B NMR spectra suggested another possible structure[94,95]: $AlH_2(NH_3)_4^+BH_2(NH_3)_2^+(BH_4)^-$. The true structure of this compound still has to be determined.

The beryllium complexes $Be(BH_4)_2.L$, where L = $O(C_2H_5)_2$, $P(CH_3)_3$, or $N(CH_3)_3$, were also studied by NMR.[96] The NMR spectra of all these compounds demonstrate the equivalence of both the protons and boron atoms. The following possible structures have been proposed for $Be(BH_4)_2.P(CH_3)_3$ on the basis of infrared spectra[97]:



However, the ^{11}B NMR spectrum of this compound show a single quintet (1 : 4 : 6 : 4 : 1), which demonstrates the equivalence of both the hydrogen atoms and ^{11}B atoms. The authors believe that the above forms can be rapidly interconverted so that average signals due to B and B′ atoms are observed.

The examples discussed show that the occurrence of proton exchange is characteristic not only of free metal tetrahydroborates but also of their neutral complexes.

VI. MIXED METAL HYDRIDES

The NMR method has been widely used to investigate the products of the various double decomposition reactions. For example, the study of the ^1H and ^{11}B NMR spectra of products of the reaction between lithium salts and aluminium tetrahydroborate established[57,93,94] that the complex anion $[Al(BH_4)_4]^-$ is formed. The ^{11}B NMR spectrum of this anion shows a quintet (1 : 4 : 6 : 4 : 1) and the ^1H NMR spectrum consists of a broad unresolved signal. The infrared spectra indicate a bridged structure, while the NMR spectra demonstrate the equivalence of all the protons. There is probably proton exchange in the anion $[Al(BH_4)_4]^-$, as in $Al(BH_4)_3$.

The formation of two complex beryllium anions, $Be(BH_4)_3^-$ and $Be_2(BH_4)_5^-$, has been reported[98]. A structure with a formally tricoordinate beryllium atom was proposed for $Be_2(BH_4)_5^-$:

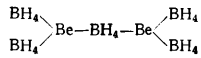


Table 6. The ^{11}B NMR parameters of certain mixed hydrides.

Compound	Solvent	δ ^{11}B	J_{B-H}	References
$LiTh(BH_4)_5$	Ether	13.4	34.5	100
$LiZr(BH_4)_5$	Ether	13.5	86	100
$LiHf(BH_4)_5$	Ether	15.4	86	100
$[(C_{16}H_{17})_3NC_9H_7][Al(BH_4)_4]$	Benzene	33.1	79	98
$[(C_{16}H_{17})_3NC_9H_7][Be(BH_4)_3]$	Benzene	34.7	80	98
$[(C_{16}H_{17})_3NC_9H_7][Be_2(BH_4)_5]$	Benzene	35.1	83	98
$LiZn(BH_4)_3$	Ether	42.3	84.5	101

The ^{11}B NMR spectra indicate the equivalence of all the tetrahydroborate groups. Table 6 presents the NMR parameters for certain mixed hydrides. The differences between the ^{11}B chemical shifts in the spectra of the above compounds are due to differences between the electronic structures of the central atoms, but all the spectra demonstrate the equivalence of the protons[99].

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Kinetic and Thermodynamic Aspects of Catalysis by Immobilised Enzymes

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The review deals with a quantitative analysis of the physicochemical characteristics of catalysis by immobilised enzymes. The role of factors such as inhibition by external and internal diffusion and the characteristics of diffusion in polymeric carriers, the nature of the carrier, the changes in the true kinetic parameters of enzymatic reactions after immobilisation, and steric limitation of the rates of reaction of immobilised enzymes with macromolecular substrates are considered. The bibliography includes 152 references.

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I. INTRODUCTION

There has been an exponential growth in recent years of the number of studies on immobilised (fixed) enzymes, which has doubled in approximately two years. According to the data of the American Chemical Society[1], research in the field of immobilised enzymes was among the nine most intensely studied topics in chemistry in 1972.

Interest in immobilised enzymes can be explained by two fundamental causes. Firstly, the wide prospects which are opened up by the application of immobilised enzymes in technology and medicine. In this connection we may point out that the unique properties of biological catalysts have been for a long time attracting the attention of workers in different branches of sciences and engineering. These properties include primarily their high catalytic efficiency (i.e. the ability to ensure reaction rates greatly exceeding, sometimes by a factor of 10^{10}—10^{13}, those in the presence of non-biological catalysts), their insurpassable selectivity (not only as regards the type of reaction catalysed but also with respect to the structure of the substrate), and finally the high capacity of enzymes to respond to the regulating action of fine changes in the properties and specific composition of the medium. However, the attempts to use biological catalysts as catalytic or regulating elements in applied chemistry or physics have as a rule encountered a seemingly insurmountable obstacle, involving their exceptionally low resistance to the denaturing influence of the "medium" (the effects of heat and micro-organisms as the principal denaturing factors in protein systems *in vitro* must be mentioned in the first place). On the other hand, the first studies in the field of immobilised enzymes have already suggested a number of ways of improving their stability[2].

1. Covalent attachment of the enzyme to a water-insoluble (or water-soluble) polymeric carrier (such as cellulose, glass, polystyrene, polyaminoacids, etc.).
2. Covalent attachment of enzyme molecules to one another with the aid of an added polyfunctional reagent with formation of water-insoluble (or water-soluble) aggregates.
3. The incorporation of the enzyme in the three-dimensional network of a gel or polymer.
4. The adsorption of the enzyme on water-insoluble carriers (for example on ion-exchange resins).
5. The inclusion of the enzyme in semipermeable microcapsules or polymeric fibres.

Evidently as a result of immobilisation of this kind the enzyme acquires yet another property important for technology—it can be readily separated from the products of the catalysed reaction, which permits its repeated employment or its use under flow conditions[3].

In medical practice immobilisation facilitates the fixation of the enzymes (or other biologically important substances) in specific parts of the organism in addition to increasing its stability[4].

Immobilised enzymes can be regarded as extremely realistic models for biologically active systems acting *in vivo* within membranes or on their surface[2,5].

A number of reviews have already been published on immobilised enzymes[2,3,6-23]. Since a compilation of these reviews has been published in Russia[24], we shall not deal with the methodological aspects of the preparation of immobilised enzymes (see, for example, Crook et al.[10] and Weetall[16]) or the practical aspects of their use in science, engineering, and medicine[3,25]. Attention is concentrated on the kinetic and thermodynamic features which distinguish catalysis by immobilised enzymes from the behaviour of homogeneous (native) systems. These new specific features may include (a) the appearance of external and internal diffusion inhibition in catalysis, (b) factors associated with the distribution of substrates, inhibitors, hydrogen ions, and other effectors between the aqueous solution and the polymeric matrix (as a result of electrostatic or hydrophobic interaction, hydrogen bonds, etc.), and (c) the occurrence of steric hindrance in reactions with macromolecular substrates. In examining these aspects, we shall endeavour to achieve quantitative generalisations, which would make it possible to predict *a priori* in many cases the kinetic and thermodynamic properties of immobilised enzymic systems.

II. THE ROLE OF DIFFUSION IN CATALYSIS BY IMMOBILISED ENZYMES

The principal postulates formulated in the theory of heterogeneous catalysis are essentially applicable to

immobilised enzymes. The effect of diffusion on heterogeneous catalytic processes has been studied in extremely great detail for reactions of different kinetic orders[26-30]. Here we shall consider the influence of diffusion factors on an enzymic reaction whose rate v obeys the Michaelis–Menten equation:

$$v = \frac{V_{max} \cdot C}{K_m + C}, \quad (1)$$

where $V_{max} = k_{cat}[E]$, $[E]$, and C are the initial concentrations of the enzyme and substrate respectively, k_{cat} the catalytic first-order rate constant, and K_m the Michaelis constant. We shall bear in mind that the reacting enzyme is in an immobilised state, being, for example, bound covalently to a water-insoluble porous carrier or incorporated in a gel matrix or within a microcapsule. For the enzymic reaction to occur, it is evidently necessary in the first place for a substrate molecule in solution to approach the surface of the particle containing the immobilised enzymes and in the second place that it can diffuse within the latter. On the other hand, if the reaction in the surface layers of the particle is faster than the supply of the substrate from the solution to the surface, then a zone depleted in the substrate will arise round the particle after a time. As a result, the overall rate of the enzymic process will be determined by the rate of mass transfer of the substrate to the particle. By analogy with heterogeneous catalysis[26], we may say that in this case the process is controlled by external diffusion. On the other hand, we can imagine that the mass transfer of the substrate is faster than the enzymic reaction on the surface of the particle. Then another type of diffusion-dependent inhibition may arise, namely, if the size of the carrier particle is very great or its enzyme is very active, then almost the entire substrate reacts in the part of the carrier near the surface, while its bulk is depleted in the substrate. In such cases one usually says that the process is controlled by internal diffusion[26]. The effects of both diffusion factors on the effective kinetic parameters of an enzymic reaction are analysed below with the framework of the Michaelis equation [Eqn. (1)].

1. EXTERNAL DIFFUSION INHIBITION

Mass transfer takes place as a result of two different processes—convection and molecular diffusion. In liquids the transport of a substance as a result of convection is usually much faster than molecular diffusion[30] and therefore the latter process may be virtually disregarded. However, in examining heterogeneous systems (for example suspended solid particles) one must bear in mind that the boundary between the "phases" is directly adjoined by a layer of unstirred liquid within which the transport of molecules or ions proceeds exclusively via molecular diffusion. Consequently, when an enzymic reaction in which the substrate is consumed takes place on the surface of the particle, a steep reactant concentration gradient may arise within the unstirred layer, because molecular diffusion in liquids is very slow (with a diffusion coefficient of 10^{-5}–10^{-6} cm^2 s^{-1}).[30] As a result, the rate of mass transfer may be limited by the stage involving the heterogeneous catalytic process regardless of the rate of stirring.

We shall consider certain quantitative features of the process for a spherical particle assuming that the enzyme is immobilised either on the surface of a sphere or, if the carrier is porous, also within the sphere, but in the absence of internal diffusion inhibition. We shall assume further that the partition coefficient of the substrate between the solution and the carrier "phase" hardly differs from unity. The surface of the particle may be regarded as equally accessible[26]. Then the rate of supply of the substrate by diffusion j, referred to unit surface area of the particle is †

$$j = \beta (C_0 - C), \quad (2)$$

where C_0 and C are the substrate concentrations in the bulk of the solution and on the surface of the particle respectively, and β is the mass transfer coefficient.

a. In the special case where the enzymic reaction occurring on the surface of the particle follows first-order kinetics we have $K_m \gg C$ in Eqn. (1). Under these conditions, the steady state in the enzymic process is described by the following equation:

$$\beta (C_0 - C) = (V_{max}/K_m) \cdot C, \quad (3)$$

which reflects the fact that the specific rate of supply of the substrate to the surface of the particle with the immobilised enzyme (j) is equal to the rate of the enzymic reaction (v) referred to the unit surface area. From Eqn. (3), we have for the effective substrate concentration in the reaction zone

$$C = \frac{\beta \cdot C_0}{\beta + V_{max}/K_m}. \quad (4)$$

As a result, we conclude that the experimental steady-state rate of the enzymic reaction

$$v = (V_{max}/K_m) \cdot C = k_{eff} \cdot C_0 \quad (5)$$

is characterised by an effective first-order rate constant given by

$$k_{eff} = \frac{(V_{max}/K_m) \cdot \beta}{\beta + V_{max}/K_m} = \frac{1}{\frac{1}{\beta} + \frac{1}{V_{max}/K_m}}. \quad (6)$$

Two limiting cases are possible. When $\beta \gg V_{max}/K_m$, i.e. the mass transfer is much faster than the chemical reaction, we have $k_{eff} = V_{max}/K_m$. On the other hand, when $\beta \ll V_{max}/K_m$, i.e. the chemical reaction is much faster than the mass transfer, then $k_{eff} = \beta$. In the first case we shall say that the reaction proceeds under kinetic conditions and in the second case under diffusion conditions[31].

b. In the general case when the enzymic process is not of first order but of a fractional order (i.e. $K_m \sim C$) the existence of two process conditions (diffusion and kinetic) still remains in force despite the more cumbersome expressions for the reaction rate[26].

c. The second extreme case of the Michaelis equation [Eqn. (1)] when $K_m \ll C$, i.e. the enzyme is saturated by the substrate, constitutes an exception. Since an enzymic reaction is zero order with respect to substrate in the general case, evidently the process cannot in principle be controlled by diffusion and it proceeds under kinetic conditions.

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† This assertion is approximate. It has been shown[30] that the diffusion flux to the absorbing sphere in a moving liquid is not distributed uniformly on its surface. It is a maximum at the point where the liquid advances to the sphere and diminishes on its rear side.

Theoretical Estimation of the Limits of the Diffusion and Kinetic Regions

Under kinetic conditions, the reaction evidently proceeds in full conformity with the laws specified by its mechanism. The situation is different under diffusion conditions where the reaction kinetics cannot yield information about the chemical mechanism, since they are determined by mass transfer parameters alone. To make a choice between these process conditions, it is necessary to estimate β and compare it, for instance in case (a) (see above), with V_{max}/K_m. For this purpose, we shall show, following O'Neill[32], how this can be done after making certain assumptions. It follows from similarity theory[26] that

$$\beta = \frac{NuD}{d}, \qquad (7)$$

where Nu is the Nusselt number, D the diffusion coefficient of the substance transported, and d the diameter of the absorbing particle. For a laminar flow of the liquid around the spherical particle and low Reynolds numbers, we have[28,28] Nu = 2. As an approximation, we shall assume that this condition holds in our system‡. Then we have from Eqn. (7)

$$\beta = \frac{2D}{d}. \qquad (8)$$

This value constitutes the lower limit. In fact, in consequence of the stirring of the system, β can be higher[26]. However, in studies with enzymes stirring is not usually very fast and therefore this effect is not very significant.

Knowing D and d, it is possible to calculate β by Eqn. (8). By comparing it [case (a)] with V_{max}/K_m, one can in principle deduce the type of conditions governing the enzymic reaction [see Eqn. (6)]. However, V_{max}/K_m must be determined from experimental data, which are already distorted by the influence of diffusion and therefore we shall indicate another, more convenient approach. Having evaluated β, it is possible to calculate the maximum rate of mass transfer and to compare it with the experimental rate of the reaction catalysed on the immobilised enzyme. If these two quantities are similar, the implication is that the reaction proceeds under diffusion conditions. On the other hand, if the observed rate of the enzymic reaction is much lower than the maximum possible rate of mass transfer, the reaction evidently proceeds under kinetic conditions. This approach is valid for any kinetic order of the enzymic reaction and we shall consider it in greater detail.

The rate of mass transfer R to any catalyst particle, which is equal to the diffusion flux multiplied by the surface area of the particle A, is defined by the following expression in accordance with Eqns. (2) and (8):

$$R = jA = \frac{2D}{d} \cdot A(C_0 - C). \qquad (9)$$

Since $A = \pi d^2$ for a sphere, it follows that

$$R = 2\pi Dd(C_0 - C). \qquad (10)$$

‡ Empirical formulae are frequently used in the literature to determine β in various heterogeneous systems under different conditions[33-35]. Our approximation should hold at not unduly high flow rates and has the advantage that β can be readily estimated numerically. In certain studies on immobilised enzymes β is determined from other equations[35,36].

The diffusion coefficient of the substrate in the liquid D, entering into Eqn. (10), can be determined experimentally in a separate experiment or estimated from different empirical correlations, provided that the substrate concentration does not exceed 10 mole %.[37] On the other hand, if the particle containing the immobilised enzyme is not spherical, then d is usually assumed equal to the diameter of the sphere whose surface area is equal to that of the particle employed.

The maximum possible rate of mass transfer R_{max} follows from Eqn. (10) for $C_0 \gg C$:

$$R_{max} = 2\pi DdC_0, \qquad (11)$$

where R_{max} is usually expressed in mole per second per particle. According to the recommendations of the International Commission on Immobilised Enzymes, the rate of reaction should be expressed in micromoles of the substrate per minute per milligram of the dry immobilised enzyme preparation[38]. Then Eqn. (11) must be transformed into

$$R^{tot}_{max} = 7.2 \cdot 10^2 \cdot \frac{DC_0}{\rho d^2}, \qquad (12)$$

where ρ is the density of the immobilised enzyme preparation expressed in g cm^{-3}, D is expressed in cm^2 s^{-1}, d in cm, and C_0 is the concentration on the molar scale.

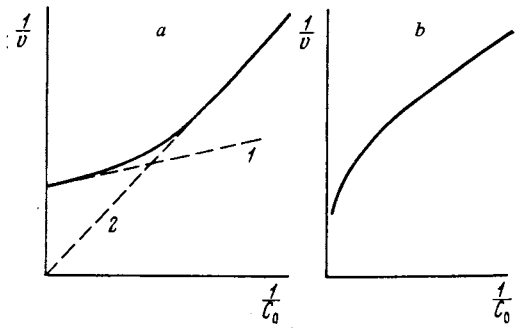

Figure 1. *a*) Theoretical variation of the rate of an enzymic reaction with substrate concentration in terms of the Lineweaver–Burk variables distorted by inhibition due to external diffusion; *b*) experimental curve in terms of the same variables[39,40] apparently corresponding to the presence of two kinetically different forms of the immobilised enzyme.

Certain Experimental Criteria

a. As mentioned above, at sufficiently high substrate concentrations (i.e. when the immobilised enzyme is saturated and the observed rate of reaction is of zero order with respect to the substrate), the enzymic process cannot in principle be controlled by the diffusion of the substrate and therefore the reaction proceeds under kinetic conditions. In its turn the probability of a transition of the reaction system to diffusion-dependent conditions increases with decrease of substrate concentration. This behaviour of the catalytic system is illustrated in Fig. 1, where the theoretical Lineweaver-Burk plot is presented for a reaction occurring at high substrate concentrations (dashed line *1*) under kinetic conditions, where

the experimental results can therefore be described with the aid of Eqn. (1), and at low substrate concentrations (dashed curve *2*) under diffusion conditions, where the variation of the experimental process velocity v with C_0 actually obeys Eqn. (12). On the other hand, if this behaviour of the $1/v-1/C_0$ plot is observed in experiments with an immobilised enzyme (i.e. the plot bends away from the usual linear Lineweaver–Burk relation), then we have the first indication that diffusion plays a significant role in the process. However, here attention should be drawn to the nature of the curvature. Thus a curved Lineweaver–Burk plot of another type, shown in Fig. 1*b*, was obtained in studies[39,40] on the catalytic properties of α-chymotrypsin and glucoamylase immobilised on cellulose derivatives. The authors also explain the observed curvature of the $1/v-1/C_0$ plot from the standpoint of diffusion-dependent inhibition. However, in this case such treatment of the results is incorrect, since it follows from theory that diffusion-dependent inhibition should be manifested particularly strongly at low substrate concentrations (Fig. 1*a*). However, the opposite behaviour actually follows from the experimental data (Fig. 1*b*), namely the process is accelerated at low substrate concentrations. Moreover, from the theoretical standpoint the process controlled by diffusion should follow first-order kinetics with respect to the substrate at low concentrations of the latter [Eqn. (12)] and this too is not observed in the experiment, since (Fig. 1*b*) extrapolation of the linear section of the $1/v-1/C_0$ curve, corresponding to low values of C_0, does not pass through the origin of coordinates. Therefore we believe that the curvature of the $1/v-1/C_0$ relation observed experimentally[39,40] (of the type of the curve in Fig. 1*b*) is probably due to the presence of several kinetically different forms of the immobilised enzyme.

b. Enzymic reactions usually have activation energies of the order of 10–30 kcal mole^{-1}. On the other hand, the rate of an enzymic process occurring under diffusion conditions should depend only slightly on temperature since the only temperature-sensitive parameter (D) in Eqn. (12) is associated with an activation energy of about 4–5 kcal mole^{-1} in water[41]. Consequently it is entirely valid to use the nature of the temperature variation of the reaction rate as a criterion for the determination of the limits of the kinetic and diffusion regions. In this connection one must, however, bear in mind that with increase of temperature the reaction undergoes a transition from kinetic to diffusion conditions [as follows, for example, from an analysis of Eqn. (6), bearing in mind the above differences between the temperature variation of β defined by Eqn. (8) and V_{max}/K_m].

c. Under diffusion conditions the reaction rate should evidently be independent of changes in the specific concentration of the immobilised enzyme [as follows, for example, from Eqns. (5) and (6)] assuming that under such conditions $V_{max}/K_m \gg \beta$. Moreover, if the reaction proceeds under diffusion conditions, its rate should not be affected by specific factors such as a change in pH or ionic strength and the addition of inhibitors or activators; in general these factors are associated with the enzymic mechanism and their influence can in principle be followed for the native catalyst. However, one should bear in mind that, for the same preparation of the immobilised enzyme, the reaction with a highly reactive substrate can proceed under diffusion conditions, while with a less reactive substrate kinetic conditions may obtain. All the postulates discussed in this section follow, for example, from an analysis of Eqns. (5) and (6) bearing in mind that the limits of the diffusion and kinetic regions are defined by the relative values of the parameters β and V_{max}/K_m.

d. Under kinetic conditions, the rate of reaction should be independent of the degree of comminution of the particles containing the immobilised enzyme (provided that there is no internal diffusion inhibition for the substrate). On the other hand, when the reaction proceeds under diffusion conditions its rate increases after comminution of the enzymic preparation, since the decrease in the particle diameter d leads to an increase of the diffusion parameter β [see Eqn. (8)].

e. The influence of diffusion factors may weaken when the rate of mass transfer of the substrate is accelerated by stirring. As already mentioned concerning Eqn. (7), this is because the parameter β depends in principle on the flow rate[30]. A very simple relation between the reaction rate and the rate of stirring can be arrived at from the standpoint of the concept of an unstirred layer, as a physically real feature, to which Fick's first law is applicable. [See, however, the objections to this approach raised by Levin[30] (p. 51) and Ioffe and Pis'men[27] (p. 113).] When the substrate concentration in the diffusion layer decreases linearly, we find that the specific rate of mass transfer $j = (C_0 - C)(D/\delta)$, where δ is the effective thickness of the stationary layer. Comparison of this expression with Eqn. (12) shows that the parameter β, which determines the type (diffusion or kinetic) of Eqn. (16) can be formulated as $\beta = D/\delta$. In its turn, it follows from hydrodynamics that the thickness of the diffusion layer diminishes with increase of the flow rate of the liquid u around the particle[30]:

$$\delta \propto u^{-n}, \qquad (13)$$

where n varies from 1/3 to 1 depending on the conditions (for example $n = 1/3$ for spherical particles or for the flow within a cylinder). This is true not only of an individual particle but also of layers of particles. Thus an increase in the rate of rotation of the stirrer in the reactor or even an increase in the flow rate of the substrate through the column should weaken diffusion-dependent control. In its turn, the dependence of the observed rate of the enzymic reaction on the rate of stirring or on the flow rate demonstrates a significant role of diffusion in this process. Presumably a significant increase in the rate of rotation of the stirrer can cause a transition from diffusion to kinetic conditions. However, the very fact that at low rates of rotation the observed reaction rate depends on stirring while at high rates of rotation such dependence is not observed, cannot alone serve as proof of a transition from diffusion to kinetic conditions, since, as shown in a study of heterogeneous reactions[42], at high rates of stirring the so called slip effect is observed, i.e. the stirrer ceases to drag the liquid with it and therefore the true flux velocities in the system do not change on further increase of the rate of rotation.

The Applications of Theoretical Postulates to the Analysis of Experimental Data

The predicted effects have been confirmed experimentally. It has been shown[39] that, with increase of the rate of stirring in a suspension of α-chymotrypsin bound covalently to KM-cellulose, the rate of enzymic hydrolysis of the ethyl ester of *N*-acetyl-L-tyrosine also increases. In its turn, the catalytic activity of columns with an immobilised enzyme rises with increase of the flow rate of

substrate solutions through them[35,36,40,43]. Fig. 2 illustrates this type of relation for the reaction of trypsin immobilised on porous glass with the *p*-nitroanilide on *N*-benzoyl-DL-arginine[35]. Experiment[40] also confirms the conclusion that there is a high probability that the reaction passes to diffusion conditions at low substrate concentrations: thus at low concentrations of starch (5%) the rate of its reaction with immobilised glucoamylase depends strongly on the flow rate through the column, while at high concentrations (30%) it is almost independent of the flow rate. It has been shown[44] that the reaction of trypsin bound covalently to the inner surface of a nylon tube with the ethyl ester of *N*-benzoyl-L-arginine is fully controlled by diffusion (even for $C_0 > 1000K_m$), the rate of reaction being proportional to the cube root of the flow rate of the substrate through the tube, as predicted by the theory [Eqn. (13)]. Bubbling of the stream of substrate with a gas, which improves the stirring within the tube, greatly increases the observed rate of the enzymic reaction.

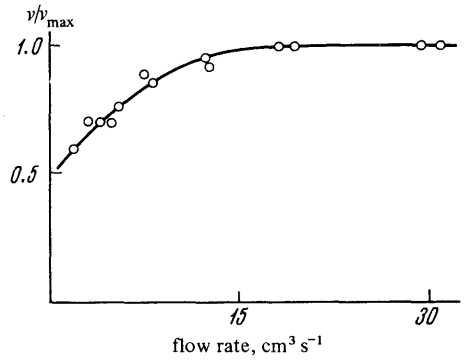

Figure 2. Dependence of the effective catalytic activity of a column filled with immobilised trypsin on the flow rate of the substrate (*p*-nitroaniline of *N*-benzoyl-DL-arginine) solution[35]; v = observed reaction rate at given flow rate Q; v_{max} = maximum reaction rate at fairly high values of Q.

Eqn. (12) can be used not only for qualitative but also for quantitative estimates of the role of external diffusion in catalysis by immobilised enzymes[32]. Thus the reaction of α-chymotrypsin immobilised on KM-cellulose and DEAE-cellulose with the ethyl ester of N-acetyl-L-tyrosine has been studied[39,45]. Table 1 presents the kinetic parameters of these reactions. In both cases the size of the particles containing the immobilised enzyme was about 40 μm and their density can be assumed to be 1 g cm^{-3}. The diffusion coefficient of the substrate, estimated with the aid of empirical correlations[46], will be assumed equal to 5×10^{-6} cm^2 s^{-1}. Then it follows from Eqn. (12) that $R^{tot}_{max} = 2.25 \times 10^2 C_0$. Consequently the maximum rate of mass transfer R^{tot}_{max} for α-chymotrypsin immobilised on DEAE-cellulose becomes lower than the calculated rate of reaction for $C_0 < 5 \times 10^{-2}$ M (as shown by the data in Table 1) and therefore diffusion should become a significant factor in the enzymic process. Indeed experiment shows[45] that the reaction is fully controlled by diffusion for $C_0 < 10^{-2}$ M and that the effect of diffusion is less significant for $C_0 > 10^{-2}$ M. Evidently the agreement between the theory and experiment is satisfactory. As was to be expected, the effect of diffusion disappears with increase of the rate of the enzymic reaction when the experiment is carried out at a pH far from the optimum (at pH < 5). In its turn, comminution of the particles containing the immobilised enzyme also lifts the diffusion-dependent inhibition[45]. The theoretical R^{tot}_{max} for α-chymotrypsin immobilised on KM-cellulose [Eqn. (12)] becomes equal to the theoretical values of v (Table 1) for $C_0 \simeq 10^{-3}$ M. It has been shown experimentally[39] that at such substrate concentrations external diffusion does indeed play an appreciable role.

Table 1. Kinetic parameters of the hydrolysis of the ethyl ester of *N*-acetyl-L-tyrosine catalysed by immobilised α-chymotrypsin.

Carrier	V_{max}, μmole/min mg of preparation	K_m, 10^{-3} M
DEAE-Cellulose (Ref.45)	12	5
KM-Cellulose (Ref.39)	0.5	1

Enzymes are sometimes immobilised in membranes[47-50] or are grafted onto cellulose sheets[51,52]. On the surface of a membrane, there is also a stationary layer, which in some cases can lead to a transition of the reaction to diffusion conditions. Such a system has been analysed in detail by Katchalski and coworkers[48]. The thickness of the diffusion layer (about 50 μm) can be found from the kinetic properties of the system. This value agrees with the earlier determinations of δ from the variation of the permeabilities of various membranes with the efficiency of stirring[53].

We may note that the examples quoted are a sufficient indication that external diffusion factors can indeed play an important role in catalysis by immobilised enzymes. The theoretical relations determined make it possible in turn to outline procedures whereby the experimenter can cause a transition of the reaction from diffusion to kinetic conditions (for example by raising the substrate concentration or conversely by reducing the specific concentration of the immobilised enzyme, or by increasing the rate of stirring, by comminuting the particles containing the immobilised enzyme, etc.).

2. INTERNAL DIFFUSION INHIBITION

The reaction of an enzyme incorporated in the three-dimensional network of a gel or a polymer or joined chemically to a porous carrier can be sensitive to inhibition by internal diffusion, i.e. the diffusion of the substrate within the gel, polymer, or the carrier pores.

We shall consider this problem in relation to a membrane (for example, a polyacrylamide[50] or collodion[47-49] membrane) or a polymeric disc (with a diameter much greater than its thickness) containing an immobilised enzyme. The problem of internal diffusion in such systems was analysed by Katchalski and coworkers[49] for low substrate concentrations and by Laidler and Sundaram[7,54] in the general case.

Here and henceforth we shall base the treatment on Fick's simple diffusion model. If there is an interaction between the membrane and the diffusing substance (for example, an electrostatic interaction[55]), then Fick's first law must be written in the form

$$\frac{dm}{dt} = -D \cdot A \cdot \left[\frac{\partial C}{\partial x} + \frac{C}{kT} \cdot \frac{\partial U}{\partial x}\right],$$

where m and C are the amount and concentration of the substance transferred, t is the time, D the diffusion coefficient, A the area through which diffusion takes place, k the Boltzmann constant, T the absolute temperature, x the coordinate of the direction of diffusion, and U the potential energy of the diffusing species, which depends on its position relative to the membrane. The solution of this equation depends on the type of the function $U(x)$. For a simple electrostatic interaction, $U(x)$ is determined by Coulomb's law.

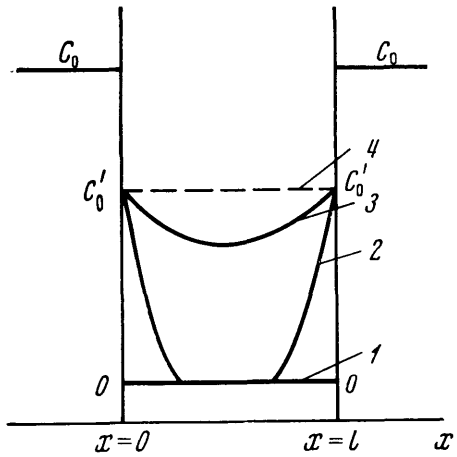

Figure 3. Diffusion of the substrate in the membrane (for explanation, see text): 1) distribution of the substrate for $t = 0$; 2) distribution of the substrate for $t > 0$; 3) steady state in the presence of enzymic reaction; 4) equilibrium state in the absence of enzymic reaction.

We place the membrane with a thickness l, on which the enzyme is immobilised, in a solution of the substrate at a concentration C_0 (Fig. 3).[7] At the initial instant ($t = 0$) the substrate concentration in the membrane is of course zero. Then it increases with time to the equilibrium value, which in the absence of an enzymic reaction is $C_0' = PC_0$, where P is the partition coefficient of the substrate between the membrane and the aqueous "phases" (dashed line in Fig. 3). On the other hand, when an enzymic reaction occurs in the membrane, consuming the substrate, then in the presence of internal diffusion inhibition the steady-state substrate concentration in the membrane may be less than C_0' and should depend on x, as shown in Fig. 3.

Time Required for the Attainment of the Steady State

For practical purposes, it is important to estimate the time required to establish the steady state where the rate of the diffusion flux becomes equal to the rate of the enzymic reaction and therefore the concentration of the substrate diffusing to the enzyme remains constant (steady-state value for C_0 = const.). In general an analytical solution of the problem is impossible and therefore it is necessary to resort to numerical methods. In this connection we shall analyse to a first approximation the case where there is no enzymic reaction in the membrane. Assuming that $P = 1$, the variation of the concentration C in the membrane with time t can be formulated thus[56]:

$$C = C_0\left[1 - \frac{2}{\pi}\sum_{n=1}^{\infty}\frac{1-\cos n\pi}{n} \cdot \sin\frac{n\pi x}{l} \cdot \exp\left(-\frac{Dn^2\pi^2 t}{l^2}\right)\right], \quad (14)$$

where D is the diffusion coefficient of the substrate in the membrane medium. For fairly long times, the sum of the series in Eqn. (14) is determined mainly by the first term ($n = 1$):

$$C = C_0\left[1 - \frac{4}{\pi} \cdot \sin\frac{\pi x}{l} \cdot \exp\left(-\frac{D\pi^2 t}{l^2}\right)\right]. \quad (15)$$

Naturally the substrate concentration is always a minimum in the centre of the membrane ($x = l/2$). It will be assumed that the time τ after the elapse of which the substrate concentration in the centre of the membrane is 90% of its initial concentration in the solution, i.e. $C = 0.9\,C_0$, corresponds to virtual attainment of equilibrium. Then we have from Eqn. (15)

$$\frac{4}{\pi} \cdot \exp\left(-\frac{D\pi^2\tau}{l^2}\right) = 0.9, \quad (16)$$

whence§

$$\tau = 0.035 \cdot \frac{l^2}{D}. \quad (17)$$

The time of the virtual attainment of the steady state can be readily estimated from Eqn. (17). The membrane thickness l can be measured. The diffusion coefficients of different (low-molecular-weight) substances in the membrane D may be assumed to differ little from the diffusion coefficients measured in water, when the polymer content in the gel is not too high (such membranes are in fact used for the immobilisation of enzymes[47-50]). Thus it is shown in Table 2 for sucrose as an example that the diffusion coefficient in a dilute gel is lower only by a factor of 2–3 compared with an aqueous medium. Ultimately, if it is assumed that $D \simeq 3 \times 10^{-6}$ cm^2 s^{-1}, which is typical for substances[57] with molecular weights up to 10^3, Eqn. (17) yields $\tau \simeq 2$ min for a membrane 1 mm thick.

On the other hand, when an enzymic reaction takes place in the membrane simultaneously with diffusion, the substrate concentration at the centre of the membrane may not reach values as high as in the absence of the reaction. Consequently the time required to attain the steady state with respect to the substrate in a membrane with an immobilised enzyme probably should not exceed the value of τ for the state of equilibrium of the membrane without the enzyme¶. Therefore τ found from Eqn. (17) can be regarded as the upper limit to the times of attainment of the diffusion steady state in enzymic membrane systems.

§ There is an arithmetical error in the derivation of Eqn. (16) from Eqn. (17) in publications by Laidler and Sundaram[7,54], which results in an incorrect expression for τ, the true value being exceeded by a factor of 7.3.

¶ Provided that of course the enzyme itself or changes induced by it in the membrane do not exhibit a significant influence on the diffusion coefficient of the substrate.

Determination of the Kinetic Parameters of an Enzymic Reaction in the Absence of Internal Diffusion Inhibition

On the other hand, if the reaction with an immobilised enzyme is slower than diffusion (because the enzyme is not very active or its specific concentration is low) so that the equilibrium distribution of the substrate between the aqueous solution and the carrier particles is not disturbed, the specific rate of reaction referred to unit volume of the carrier should be represented as follows according to Eqn. (1):

$$v_{sp.} = \frac{k'_{cat}[E]_M C'_0}{K'_m + C'_0}, \quad (18)$$

where $C'_0 = PC_0$, $[E]_m$ is the concentration of the enzyme in the bulk of the carrier, and k'_{cat} and K'_m are the true kinetic parameters of the enzymic process within the carrier, which may differ in principle from the corresponding parameters for the reaction in water if only because the enzyme can assume, as a result of being immobilised, a conformation different from that in water or because of the influence of the medium. Hence the overall rate of reaction, referred to the entire bulk of the carrier (v_{tot}, mole s^{-1}), can be formulated as follows:

$$v_{tot} = \frac{k'_{cat.} EC_0}{K_{m(obs.)} + C_0}, \quad (19)$$

where $K_{m(obs)} = K'_m/P$, E is the total amount of the enzyme in the carrier equal to $[E]_M Al$ for a membrane, A is the area of one side of the membrane, and l is its thickness. Eqn. (19) shows that the kinetic parameters k'_{cat} and K'_m can be found by the usual procedure used in enzyme kinetics for the analysis of the Michaelis equation, provided that P is determined in an independent experiment.

Table 2. Diffusion coefficients D of sucrose in different media.

Medium	$10^6 D$, $cm^2 s^{-1}$	Refs.
Aqueous solution	5.0	58
9.5% polyacrylamide gel (95% acrylamide + 5% cross-linking agent[a])	2.5 ± 0.7	59
9.9% polyacrylamide gel (90% acrylamide + 10% cross-linking agent[a])	1.9 ± 0.7	59
7.2% polyacrylamide gel (99% acrylamide + 1% cross-linking agent[a])	3.5 ± 0.2	59
7% gelatin gel	1.5 ± 0.2	60
0.8% agar-agar gel	2.5 ± 0.5	61
Collodion membrane containing 90% of water	2.8	47

[a] *NN'*-Methylenebisacrylamide.

Effect of Internal Diffusion on the Effective Values of the Kinetic Parameters of an Enzymic Reaction in the Membrane

One can be by no means always certain that the occurrence of the enzymic reaction does not disturb the equilibrium in the distribution of the substrate between water and the carrier. In the general case a substrate concentration C at a specified point in the membrane (with the coordinate x, see Fig. 3) is defined by the equation for the steady-state:

$$D \cdot \frac{d^2C}{dx^2} = \frac{k_{cat.}[E]_M C}{K'_m + C}, \quad (20)$$

which in fact reflects the equality of the gradient of the diffusion flux through unit surface area, defined by Fick's second law, and the rate of the enzymic reaction. The problem consists of finding the form of the function $C(x)$. Generally speaking, Eqn. (20) can be solved only numerically with the exception of two cases.

a. If $C \ll K'_m$ (this is true, for example, at low substrate concentrations when $C'_0 = C_0 P \ll K'_m$), then

$$\frac{d^2C}{dx^2} = \alpha^2 C, \quad (21)$$

where

$$\alpha = \sqrt{\frac{k'_{cat}[E]_M}{K'_m D}}. \quad (22)$$

The solution of Eqn. (21) by Euler's method with the boundary conditions $x = 0$, $C = C'_0$, $x = l$, and $C = C'_0$ yields

$$C = C'_0 \cdot \frac{\sinh \alpha x + \sinh \alpha (l - x)}{\sinh \alpha x}. \quad (23)$$

The steady-state rate of consumption of the substrate in the system must be equal to the diffusion flux through both sides of the membrane, i.e.

$$v'_{tot.} = 2AD \frac{dC}{dx}\Big|_{x=0,l}, \quad (24)$$

where the substrate concentration gradient at the boundary of the membrane follows from Eqn. (23) and is given by

$$\frac{dC}{dx}\Big|_{x=0} = \frac{dC}{dx}\Big|_{x=l} = \pm \alpha C'_0 \cdot \frac{\cosh \alpha l - 1}{\sinh \alpha l}. \quad (25)$$

Then, after simple rearrangement, the overall rate of reaction, referred to the entire volume of the carrier (v'_{tot}) or its specific value (v'_{sp}) per unit volume carrier, can be formulated as follows on the basis of Eqn. (24) and (25):

$$v'_{sp} = \frac{v'_{tot}}{Al} = \frac{k'_{cat}[E]_M C'_0}{K'_m} \cdot F, \quad (26)$$

where

$$F = \frac{2}{\alpha l} \cdot \frac{\cosh \alpha l - 1}{\sinh \alpha l} \equiv \frac{\tanh \gamma}{\gamma}, \quad (27)$$

and $\gamma = \alpha l/2$. Evidently Eqn. (26) differs from Eqn. (18) for the rate of reaction in the absence of diffusion-dependent inhibition (subject to the condition that $C'_0 \ll K'_m$) only by a factor F, which in fact reflects the effect of internal diffusion. F is called the efficiency factor; its properties will be discussed in greater detail below. Here we shall only consider Fig. 4, where F is plotted against αl calculated on the basis of Eqn. (27). When $\alpha l \to 0$ {this holds for a very low enzyme activity $k'_{cat}[E]_M/K'_m$ or for a thin membrane}, we have $F \to 1$, as expected from general considerations. With increase of the thickness of the membrane l or with increase of the activity of the immobilised enzyme {$k'_{cat}[E]_M/K'_m$, see Eqn. (22)}, F falls, which indicates a growing influence of diffusion-dependent inhibition.

b. When $C \gg K'_m$ (this happens when C'_0 is so large that the steady-state substrate concentration at any point in the membrane is much greater than K'_m), we have from Eqn. (20)

$$\frac{d^2C}{dx^2} = \omega, \quad (28)$$

where $\omega = k'_{cat}[E]_M/D$. Subject to the boundary conditions $x = 0$, $C = C'_0$, $x = l$, and $C = C'_0$, the solution of Eqn. (28) becomes

$$C = C'_0 - \frac{1}{2}\omega x(l - x) . \quad (29)$$

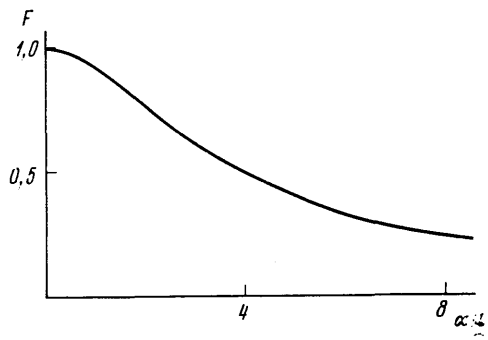

Figure 4. Theoretical variation of the F-factor with αl [Eqn.(27)].

As stated above, under steady-state conditions the overall rate of consumption of the substrate, referred to the entire volume of the carrier, must be equal to the diffusion flux through both sides of the membrane [see Eqn. (24)]. Since the substrate concentration gradient at the boundary of the membrane, derived from Eqn. (29), is

$$\left.\frac{dC}{dx}\right|_{x=0} = \left.\frac{dC}{dx}\right|_{x=l} = \pm\frac{1}{2}\omega l , \quad (30)$$

it follows that Eqn. (24) can be rewritten thus:

$$v'_{tot} = \omega ADl = k'_{cat}[E]_M Al . \quad (31)$$

Evidently the last expression is the same as Eqn. (18) (when $C'_0 \gg K'_m$), which holds for the rate of reaction in the absence of diffusion-dependent rate limitation. This implies that diffusion does not play any role in the enzymic reaction at fairly high substrate concentrations ($C \gg K'_m$).

c. We shall now consider the general case where $C \simeq K'_m$. As already stated, in the general case Eqn. (20) can be solved only numerically. However, the nature of the variation of the rate of the enzymic reaction v'_{tot} with substrate concentration in the solution C_0 can be represented qualitatively on the basis of Eqns. (26) and (31) characterising cases (a) and (b). If the rate of reaction obeys the Michaelis–Menten equation

$$v'_{tot} = \frac{k'_{cat\,(obs.)}EC_0}{K'_{m(obs.)} + C_0} , \quad (32)$$

over the entire experimental range of substrate concentrations, then on the basis of Eqn. (26) and (31) one may assume that

$$k'_{cat\,(obs.)} = k'_{cat} \text{ and } K'_{m\,(obs.)} = \frac{K'_m}{P \cdot F} . \quad (33)$$

Although the above reasoning is not entirely rigorous, the conclusions reached on its basis are satisfactorily confirmed by the results of the numerical integration of Eqn. (20).[7]

It is seen from Eqn. (33) that internal diffusion in no way affects the effective catalytic rate constant and influences only the observed Michaelis constant. The calculation based on Eqn. (27) shows that, when $\alpha l < 1$, F differs from unity by not more than 10%, i.e. $K'_{m(obs)} \simeq K'_m/P$, as predicted by Eqn. (33), and consequently diffusion does not have an appreciable influence on the reaction. On the other hand, when $\alpha l > 1$, F is significantly smaller than unity, i.e. $K'_{m(obs)} > K'_m/P$ and therefore diffusion of the substrate plays a significant role. Thus, in order to estimate beforehand the possible influence of internal diffusion on catalysis by an enzyme immobilised in a membrane, it is useful to calculate F [Eqn. (27)], on which the effective Michaelis constant depends [Eqn. (33)], and to compare it with unity. When $\alpha l > 3$, one can put approximately

$$F \approx \frac{2}{\alpha l} , \quad (34)$$

(see also Fig. 4). For an approximate estimate, it is useful to assume that k'_{cat} and K'_m, which determine the values of α [Eqn. (22)], differ little from the kinetic parameters of the reaction in water. A test of the theory carried out in Laidler's[50] and Katchalski's[49] laboratories fully confirmed this.

Certain Characteristics Distinguishing Rate Limitation by Internal Diffusion from Rate Limitation by External Diffusion

a. For very high values of αl, when $F \ll 1$ [Eqn. (4)] and therefore the reaction is significantly retarded by diffusion [Eqns. (32) and (33)], we have $K'_{m(obs)} \gg C_0$. In this case we obtain the following expression from Eqns. (22), (26), and (34) for the overall rate of the enzymic process referred to the entire volume of the carrier:

$$v'_{tot} = 2PC_0\sqrt{\frac{k'_{cat}[E]_M D}{K'_m}} . \quad (35)$$

It is seen from Eqn. (35) that, in contrast to rate-limitation by external diffusion, where the reaction rate under diffusion conditions is altogether independent of the catalytic properties of the enzyme [see, for example, Eqns. (5) and (6)], when the rate is limited by internal diffusion it is proportional to the square root of the enzyme concentration and enzyme activity.

b. In contrast to rate limitation by external diffusion, where the temperature variation of the reaction rate under diffusion conditions reflects only the activation energy governing the diffusion coefficient (see p. 12), when the rate is limited by internal diffusion [Eqn. (35)], the apparent activation energy ϵ_{app} depends on the temperature variation of not only the kinetic and diffusion parameters ($\sqrt{k'_{cat}/K'_m}$ and $\sqrt{D}$ respectively) but also of the partition coefficient P of the substrate between water and the carrier in the following way: $\epsilon_{app} = \frac{1}{2}(\epsilon + \epsilon_D + 2\Delta H_p)$, where ϵ is the activation energy for the enzymic reaction, ϵ_D the activation energy for the diffusion of the substrate, and ΔH_p the enthalpy of its transfer from water to the carrier.

c. It is interesting to note that the inhibition of the enzymic reaction diminishes the influence of internal diffusion in catalysis[62]. This follows from an analysis of Eqn. (34) bearing in mind that in the inhibition the values

of k'_{cat} and K'_m, which determine α[Eqn. (22)], are in fact effective quantities, which depend on the inhibitor concentration in the usual way.

Dependence of Internal Diffusion on the Geometrical Properties of the Particle

The influence of internal diffusion on the reaction between the substrate and the enzyme immobilised in the membrane was discussed above. However, the particles containing the immobilised enzyme usually have a spherical, cylindrical, or other shape. Naturally it is possible in principle to carry out a similar analysis in each of these instances[62,63]. However, we believe that it is far more useful to consider immediately a more universal case.

Suppose that we have a particle in which the enzyme molecules are distributed uniformly in the matrix (gel, polymer, or porous carrier). The substrate must diffuse into the particle (as before, external diffusion is regarded here as a factor which has been taken into account) and reacts there. The solution of this problem is analogous to that considered by Zel'dovich[64], Thiele[65], and Damköhler[66] for heterogeneous catalysis. They showed that the observed rate of the catalytic reaction controlled by diffusion is

$$v_{obs} = \eta v, \qquad (36)$$

where v is the rate of reaction in the absence of diffusion control, η the efficiency factor[65], which depends on the parameter Φ:

$$\Phi = a\sqrt{\frac{v}{C_0 D}} \qquad (37)$$

(Thiele's modulus), where a is the particle size (the radius for a sphere), C_0 the concentration of the reactant in the bulk phase, and D its diffusion coefficient within the catalyst particle. The specific form of the function η depends on the shape of the particle and the order of the reaction with respect to the substrate†. However, Aris[67] showed that the shape of the particles has only a slight influence on the function η. In all cases the curve relating η to Φ resembles closely the analogous curve for the relation between F and αl (Fig. 4). With increase of the reaction order from zero to third, the $\eta-\Phi$ curve in Fig. 4 is only a little displaced to the left and is slightly deformed. However, the following fact remains unaltered: when $\Phi < 1$, then η is close to unity and therefore diffusion is not important for the process; on the other hand, when $\Phi > 1$, then $\eta < 1$ and the reaction is retarded by diffusion. Therefore presumably the parameter αl, characterising the internal diffusion in the membrane, is a special case of Thiele's modulus. Consequently, in order to estimate beforehand the role of internal diffusion in the immobilised enzyme system[68], it is merely necessary to calculate Φ and compare the corresponding value of η with unity.

In the calculation of Φ [Eqn. (37)] account must be taken of the fact that the substrate diffusion coefficient in the porous particle (for example in porous glass)[28] is $D = D_{true}q$, where D_{true} is the true diffusion coefficient of the substrate in the liquid filling the pores of the particle and q is the fraction of the pore volume (i.e. the space available for diffusion) relative to the total volume of the particle. For example, in the diffusion of oxygen dissolved in water into the pores of porous glass[36] $D_{true} = 2.4 \times 10^{-5}$ cm^2 s^{-1} and $D = 0.93 \times 10^{-5}$ cm^2 s^{-1}, i.e. $q = 0.39$.

† For example, for a unimolecular reaction involving a plate, we have $\eta = (1/\Phi)\tanh\Phi$ and for a sphere we have $\eta = (1/\Phi)(1/\tanh 3\Phi - 1/3\Phi)$.[27,28]

Practical Application of Theoretical Relations

The proposed theory suggests ways of decreasing the rate limitation by internal diffusion in catalysis by immobilised enzymes—see, for example, Eqns. (32)–(34) or (36)–(37). There are two main procedures: the first, which is the most effective, involves a decrease of the particle size of the immobilised enzyme and the second involves a decrease of the specific enzyme concentration in the particle. As an example, Fig. 5 presents the experimental relation between η and Φ for glucose oxidase immobilised on porous glass[36], observed when the particle size is altered. It is found that η reaches about 0.95 only for a particle size of about 30 μm.

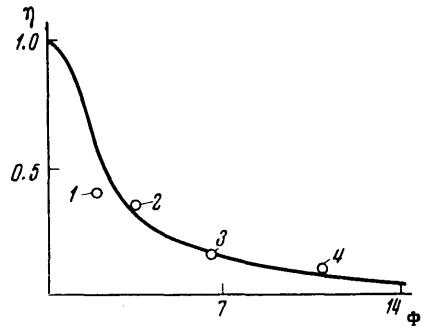

Figure 5. Variation of η with Φ. The curve was calculated theoretically and the circles represent experimental values for the given particle size (μm):[36] 1) 125–250; 2) 250–500; 3) 500–1000; 4) >1000.

With the aid of the theory described above, it is possible to predict the most favourable (from the standpoint of the absence of rate limitation by internal diffusion) immobilisation procedures. Thus analysis showed that[69], for a given particle size of the carrier and a constant amount of the deposited enzyme, Φ is smaller (and therefore η is closer to unity) when the enzyme is not distributed uniformly throughout the bulk of the carrier, but forms instead a surface film on a catalytically inert grain. This method for immobilising enzymes is in fact used successfully[70,71].

It is interesting to note that, as shown theoretically[72,73] and confirmed experimentally[74,75], in immobilised polyenzyme systems, where the reaction product of one enzyme is the substrate of another, the presence of rate limitation by internal diffusion can lead to an increase of the overall rate of reaction. This is because rate limitation by internal diffusion leads to the "concentration of the product" (i.e. of the substrate of the next reaction) in the bulk of the carrier relative to the equilibrium distribution.

3. DIFFUSION IN SIMPLE LIQUIDS AND POLYMERS

When enzymes are immobilised in polymeric carriers and also when they are enclosed in polymeric (usually polyamide) microcapsules[76–86] or in hollow fibres[87–89] there arises the problem of diffusion of the substrate through the polymeric medium.

According to the theory of Lieb and Stein[90-92], developed in recent years, the diffusional behaviour of non-electrolytes in simple liquids and in polymers can differ radically. In the diffusion in simple liquids the particle size of diffusing substances is as a rule greater than the molecular size of the diffusion medium, which therefore may be regarded as continuous and isotropic with respect to viscosity. On the other hand, in the diffusion of molecules into polymers, the molecular size of the diffusing substance is smaller than the molecular dimensions of the diffusion medium. Since diffusion in polymers proceeds via the motion of segments of polymeric molecules of the medium, the latter cannot be regarded as homogeneous and isotropic with respect to viscosity.

For a spherical diffusing species with a radius a in a simple liquid, the diffusion coefficient is defined by the Stokes–Einstein equation:

$$D = \frac{kT}{6\pi a \nu}, \qquad (38)$$

where k is the Boltzmann constant, T the absolute temperature, and ν the viscosity of the diffusion medium. If it is assumed that the diffusing molecules are spheres with a constant density, Eqn. (38) can be transformed into

$$D M^n = \text{const}, \qquad (39)$$

where M is the molecular weight of the diffusing substance and n a numerical coefficient equal to 1/3 for spherical molecules. This approximation is valid for many large protein molecules, although usually the molecules cannot be regarded as spherical and therefore n differs somewhat from 1/3. As an example, Table 3 presents the diffusion coefficients for various non-electrolytes in water[41], $n = 0.43$ follows from a plot of $\lg D$ against $\lg M$ on the basis of these data. Analysis of extensive data[91] has shown that in simple liquids n varies from 0.3 to 0.5, i.e. the diffusion coefficient depends only fairly slightly on the molecular weight of the diffusing substance.

Table 3. Diffusion of different non-electrolytes in water[41].

Diffusing substance	$10^6 D_{25°}$, cm^2 s^{-1}	Activation energy for diffusion ϵ_D, kcal mole^{-1}
Urea, $M = 60$	13.78	4.470
Glycine, $M = 75$	10.55	4.627
Alanine, $M = 89$	9.097	4.783
Glucose, $M = 180$	6.728	4.959
Cyclohepta-amylose, $M = 1134$	3.224	4.931
Bovine serum albumin, $M = 68000$	0.65	4.969

In polymers diffusion proceeds via "holes" formed at random as a result of the thermal motion of polymeric segments[93]. In order that the diffusing substance can pass through the holes, it must evidently have suitable dimensions. Diffusing species comprising very small species can pass through both small and large holes, while those with large species can only penetrate large holes. Since the formation of large holes requires more energy, their number is smaller than that of very small holes; this qualitative reasoning is confirmed by quantitative calculations[91]. Therefore the diffusion coefficients of small and large molecules in polymeric media should presumably differ sharply, i.e. n is large. Indeed, we have, for example, $n = 3.8$ for poly(methyl methacrylate) as a diffusion medium at 65°C.[90,94] Whereas in diffusion in the usual liquids doubling of the molecular weight leads to a decrease of D by a factor of about 1.4,[41] in diffusion in poly(methyl methacrylate) this leads to a 14-fold diminution of D! For different polymeric media, n varies from 2 to 8.[95-97]

Analysis of the effect of molecular shape on the diffusion coefficient showed that, for example, in water when the molecular shape deviates from the sphere, D diminishes and is correlated with the maximum change in the molecule[98]. On the other hand, in polymeric media the diffusion coefficients of substances are correlated with the smallest changes in their molecules (Table 4), which is also apparently associated with the "hole" mechanism of the diffusion process in polymers.

Table 4. Dependence of the diffusion coefficients of hydrocarbons in polyisobutylene on their molecular geometry[99].

Diffusing substance	n-Pentane	Isopentane	Neo-pentane
$10^9 D_{35°}$, cm^2 s^{-1}*	2.64	1.32	0.62

*D was determined by extrapolating the experimental data to zero concentration of the diffusing substance.

It follows from Table 3 and the literature[57,91,100] that, firstly, the diffusion coefficient depends only very slightly on temperature (for example, the activation energy for diffusion $\epsilon_D \simeq 4-5$ kcal mole^{-1} in water) and, secondly, ϵ_D is almost independent of the molecular weight of the diffusing substance. These findings are quite understandable, since the diffusion process in simple liquids is determined mainly by the properties of the diffusion medium and not by those of the diffusing substance itself[101] (see also the Stokes–Einstein equation). On the other hand, in diffusion in polymers the values of ϵ_D exceed significantly those characteristics of solutions[102] and furthermore, ϵ_D increases appreciably with increase of the molecular weight of the diffusing substance (see Table 5). This can also be accounted for within the framework of the "hole" concept of diffusion in polymers, since the formation of large holes, necessary for the diffusion of large molecules, requires more energy than the formation of very small holes. Thus, in contrast to the diffusion in liquids, in polymers D depends strongly on temperature.

Finally, we may note that at not unduly high concentrations of diffusing substances, their joint diffusion in simple liquids is independent. On the other hand, in diffusion in polymers the addition of small amounts of certain substances (called plasticisers) leads to a sharp increase of the diffusion coefficients of other substances[97,103,104], probably in consequence of the improvement of their solubility in the polymer[104]. For example, the addition of 2% of water to a specimen of poly(vinyl acetate) at 40°C leads to an increase of the diffusion coefficient of carbon tetrachloride by a factor of 75.[103]

The data quoted show that diffusion processes in simple liquids and in polymers are fundamentally different. Lieb and Stein[97] suggested that the diffusion in liquids be

assigned to the *s*-type (from the English word 'simple') and that in polymers to the *p*-type (from the English word 'polymer'). As we have already stated, diffusion processes of the *s*- and *p*-types differ significantly in terms of four characteristics, which are compiled in Table 6.

Table 5. Diffusion of different substances into a poly-(vinyl acetate) film[97].

Diffusing substance	$10^{12}D_{40^\circ}$, $cm^2\ s^{-1}$*	ϵ_D, kcal $mole^{-1}$
Water	$1.2\cdot10^5$	15±1
Methanol	$1.5\cdot10^3$	21±2
Acetone	$1.3\cdot10^1$	39±3
1-Propanol	$4.8\cdot10^{-}$	41±4

*D was determined by extrapolating the experimental results to zero concentration of the diffusing substance.

The set of these four characteristics constitutes a criterion for the determination of the type of diffusion in the given medium. It was found[91,92] that non-mediated diffusion of non-electrolytes in biological membranes belongs fully to the *p*-type.

Table 6. Effect of various parameters on diffusion of *s*- and *p*-type[92].

Parameter	Diffusion of *s*-type	Diffusion of *p*-type
Molecular size of diffusing substance	Increase in size entails only a slight decrease of diffusion coefficient (n = 0.3–0.5)	Increase in size leads to a sharp decrease of diffusion coefficient (n = 2–8)
Molecular shape of diffusing substance	Diffusion coefficient is correlated mainly with the maximum dimension of the diffusing molecule	Diffusion coefficient is correlated mainly with the minimum dimension of diffusing molecule
Temperature	Increase of temperature leads to a slight increase of diffusion coefficient for both large and small molecules	Increase of temperature leads to an appreciable increase of diffusion coefficient—greater the greater the molecular size of diffusing substance
Plasticisers	Almost without effect	Their addition to polymeric medium leads to increase of the diffusion coefficients of other molecules

In catalysis by enzymes immobilised in polymeric matrices or microcapsules or in the diffusion of substrates (even low-molecular-weight substrates) through a polymeric medium, there is apparently also a possibility not only of *s*-type but also of *p*-type diffusion. For example, the results obtained by Mogenson and Vieth[105], who found that the permeability of a cellulose nitrate capsule to hydrogen peroxide exceeds the permeability of the same microcapsule to urea by a factor greater than twenty, can be explained only from this standpoint. In this connection we emphasise that in *p*-type diffusion one may expect a sharp dependence of the observed efficiency of catalysis on the molecular weight of the substrate and on temperature.

4. DEPENDENCE OF THE REACTION RATE CONSTANT ON THE DIFFUSION PROPERTIES OF THE MEDIUM

Even if account is taken of external and internal diffusion in an enzymic reaction, its rate may depend on the diffusion properties of the reaction medium. The problem of the effect of diffusion on the rate constants for chemical reactions was solved by Smoluchowski[106], Debye[107], and Noyes[108]. Evidently diffusion should not play any role in unimolecular reactions. For a bimolecular reaction between two uncharged species, the observed rate constant k_{obs} is given by the following general expression:

$$k_{obs} = \frac{k}{1 + \frac{k}{4\pi \cdot D_\Sigma \cdot \sigma}}, \qquad (40)$$

where k is the true reaction rate constant, D_Σ the sum of the diffusion coefficients of the reactants, and σ the equilibrium interaction distance. If $1 \gg k/4\pi D_\Sigma\sigma$, then $k_{obs} = k$ and diffusion is unimportant for the reaction; on the other hand, if $1 \ll k/4\pi D_\Sigma\sigma$, then $k_{obs} = 4\pi D_\Sigma\sigma$ (i.e. is independent of k)‡ and the reaction is fully controlled by diffusion. Eqn. (40) is valid, provided that the molecules do not interact when the distance between them (r) is greater than σ.

In general the Debye equation is valid:

$$k_{obs} = \frac{k}{1 + \frac{k\int_\sigma^\infty \exp\left(\frac{U}{kT}\right)\cdot\frac{dr}{r^2}}{4\pi D_\Sigma}}, \qquad (41)$$

where U is the energy of the interaction between the reactant species. If $U = 0$ when $r > \sigma$, Eqn. (41) becomes identical with Eqn. (40). The form of the function $U(r)$ is usually unknown and therefore Eqn. (41) cannot be put in an analytical form. However, if it is assumed that there is electrostatic Coulombic interaction between the species, then $U = z_1z_2e^2/\kappa\sigma$, where z_1e and z_2e are the charges of the reactant species (e is the electronic charge), and κ the dielectric constant of the medium. In this case we have the following expression for the rate constant for a diffusion-controlled reaction:

$$k_{obs} = 4\pi D_\Sigma \cdot \sigma \cdot \frac{\theta}{\exp\theta - 1}, \qquad (42)$$

where $\theta = z_1z_2e^2/\kappa\sigma kT$. Consequently, knowing the corresponding parameters of the medium and the reaction, it is possible to determine the limits of the region of diffusion control.

The formation of the Michaelis complex must be regarded as the fastest stage of enzymic reactions: the rate constants for this stage sometimes approach the values characteristic of diffusion-controlled processes even in water[109]. Therefore, in very viscous media, where D is exceptionally small, the reaction may be presumably fully diffusion-controlled[110] [it must be emphasised that under these conditions k_{obs} may be very small and k is proportional to D_Σ—see Eqn. (40)].

Consider the reaction of an enzyme and a substrate in the gel, assuming that the process is not controlled by diffusion in solution. With increase of the gel concentration, its pores diminish and a time must come when they

‡ This expression is valid to within the steric factor, since Eqns. (40) and (41) were derived on the assumption that each collision of the reactant leads to chemical reaction.

become comparable to the dimensions of the protein globule of the enzyme, which leads to a sharp fall of its diffusion coefficient (there is a transition from diffusion of *s*-type to *p*-type). The occurrence of this phenomenon has been established experimentally[111]. However, in a reaction with a low-molecular-weight substrate this does not lead to diffusion control even if the enzyme is completely "arrested", since Eqns. (40)—(42) include the sum of the diffusion coefficients and, furthermore, for low-molecular-weight substances D changes little with increase of the gel concentration even to very high values[59]. The situation is different when the substrate is a high-molecular-weight compound. Then an increase in the gel concentration ultimately drives the reaction towards diffusion-controlled conditions and, on further increase of the gel concentration (which entails a decrease of D), there should be a sharp decrease of the observed reaction rate. These effects were predicted and observed experimentally in our laboratory[111,112]. Fig. 6 presents data for the variation of the observed rate of reaction of trypsin with chymotrypsinogen ($M \simeq 25\,000$ for both proteins) in a polyacrylamide gel as a function of the gel concentration[112]. Evidently, with increase of the gel concentration to approximately 32%, the observed rate of reaction actually increases somewhat (which is related to its specific features) and then falls almost to zero on further increase of the concentration by only 2% owing to retardation by diffusion.

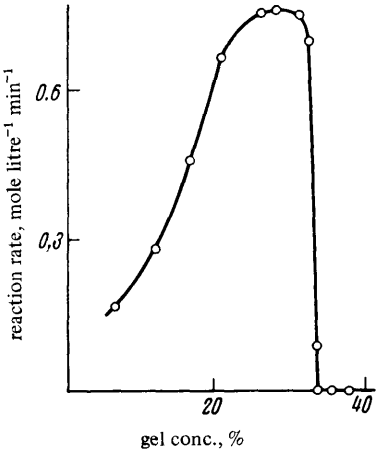

Figure 6. Variation of the observed rate of reaction ($\times 10^6$) of trypsin with chymotrypsinogen in polyacrylamide gel with its concentration[112].

In conclusion we may note that the rate of an enzymic reaction in a polymer may be controlled by diffusion even for a low-molecular-weight substrate, provided that its diffusion is of the *p*-type. In turn one should note that the retardation of enzymic reactions in polymeric (gel) media by diffusion may be used to investigate the fine structure of the polymeric matrix.

III. EFFECT OF THE NATURE OF THE CARRIER ON THE KINETICS OF REACTIONS CATALYSED BY IMMOBILISED ENZYMES

The main idea of this and the next two sections in the present review is that immobilisation of enzymes entails the actual appearance of a new type of specificity of the latter compared with the native biocatalyst. This phenomenon is due to the influence of the carrier on the catalytic process. In the first place one should note that the reaction system [consisting of the enzyme immobilised on (or in) the carrier placed in an aqueous solution] may be regarded as a two-phase system. The fact that the reaction components (substrates, cofactors, inhibitors, hydrogen ions, etc.) are uniformly distributed between the aqueous solution and the effective volume of the carrier (to which an adjacent layer of the solution should be assigned in the general case) is related precisely to the two-phase nature of the reaction system. Naturally such distribution influences the kinetics of the enzymic process. We shall consider this problem in somewhat greater detail.

1. pH EFFECTS

When the enzyme is immobilised on a charged carrier, one may expect that the concentration of hydrogen ions in the carrier phase will be smaller than in the solution if the carrier is charged positively and, conversely, will be greater for a negatively charged carrier. This follows from the quantitative theory developed by Goldstein et al.[113] Thus the ratio of the hydrogen ion concentrations in the carrier $[H^+]'$ and the solution $[H^+]$ is determined by the Boltzmann factor

$$P_{H^+} = \frac{[H^+]'}{[H^+]} = \exp\left(-\frac{e\psi}{kT}\right), \qquad (43)$$

where P_{H^+} is the partition coefficient, e the absolute electronic charge, ψ the electrostatic potential of the charged immobilised enzyme species, k the Boltzmann constant, and T the absolute temperature. As a result, the difference between the pH of the carrier and the solution is

$$\Delta pH \equiv pH' - pH = 0.43 \cdot \frac{e\psi}{kT}. \qquad (44)$$

The resulting pH shift can in turn influence the rate of the enzymic reaction, provided that the mechanism is associated with the dissociation of an ionogenic group in the enzyme or other reaction components (see the general theory of the pH effects in enzymic catalysis[114]). The dissociation constant of the ionogenic group BH^+ of the native enzyme $K = [B][H^+]/[BH^+]$ is by definition the value of $[H^+]$ for which the ionogenic group is half-neutralised. Consequently, on the basis of Eqn. (44), the pK shift due to the carrier is

$$\Delta pK \equiv pK' - pK = -0.43 \cdot \frac{e\psi}{kT}, \qquad (45)$$

where K' is the dissociation constant of the ionogenic group BH^+ in the enzyme joined to the charged carrier. It follows from Eqn. (45) that p$K' <$ pK for a positively charged carrier ($\psi > 0$) and, when the carrier is negatively charged ($\psi < 0$), then p$K' >$ pK.

Experiment confirms the above considerations. Thus at low ionic strengths the pH dependence of the catalytic activity of polyanionic trypsin derivatives is such that its optimum is displaced to the alkaline region and for polycationic trypsin derivatives it is displaced to the acid

region[13,113]. Similarly the pK of the imidazole group of the histidine-57 residue forming part of the active centre of α-chymotrypsin is 6.70 ± 0.02 for the native enzyme, 7.82 ± 0.05 for the polyanionic derivative of α-chymotrypsin, and 6.10 ± 0.05 for the polycationic derivative[115]. The list of similar factors can be extended. Thus when α-chymotrypsin[116,117], phosphatase[118], and urease[119] are immobilised on negatively charged carriers (bentonite or kaolin), the pH optimum shifts to the alkaline region. On the other hand, following immobilisation on positively charged DEAE-cellulose, the pH optima of aminoacylase[120] and invertase[121] are displaced to the acid region. Derivatives of other enzymes (papain[9], ficin[122], and subtilopeptidase A [9]) behave similarly.

The shifts of the reaction rate–pH curves described above become considerable only at a low ionic strength of the solution. This finding is explained by the fact that an increase in ionic strength as well as an increase in the dielectric constant decreases the electrostatic interaction between the charged species and hence the repulsion between the charged carrier and the effector (in the present case hydrogen ions)[123]. Table 7 lists the pK shifts for the ionogenic group controlling the catalytic activity of trypsin immobilised on a polyanionic carrier (a copolymer of ethylene and maleic acid) at different ionic strengths of the solution[113].

Table 7. Dependence of ΔpK and ψ on the ionic strength of the solution for trypsin immobilised on a polyanionic carrier[113].

Ionic strength, M	$\Delta pK \equiv pK' - pK$	Ψ, mV	Ionic strength, M	$\Delta pK \equiv pK' - pK$	Ψ, mV
0.006	−2.4	−150	0.2	−1.3	−80
0.010	−2.0	−120	1.0	−0.4	−30
0.035	−1.6	−100			

pH effects of this type occur also when the enzyme is immobilised on (or in) an uncharged carrier where one may also expect a distribution of hydrogen ions between the solution and the bulk of the carrier, namely $[H^+]' = P_{H^+}[H^+]$. Hence $\Delta pK = -\lg P_{H^+}$. This relation makes it possible to determine beforehand the sign and magnitude of the pH effects in the above systems, provided that the partition coefficient P_{H^+} is known.

The above elementary theory describes the shifts of the pH profiles not only for truly immobilised biocatalysts but also for water-soluble modified enzymes, for example for acetylated and succinylated derivatives of trypsin and α-chymotrypsin, in which the negative charge of the globule has been increased in consequence of the acylation of the amino-groups[13,17,113,124,125]. In certain cases the observed shift of the pH optimum of the reaction catalysed by the immobilised enzyme does not correspond to equilibrium and is due to the fact that there is not sufficient time for the diffusion of the acid or base formed in the reaction away from the carrier[47,49,126].

2. DISTRIBUTION OF THE SUBSTRATE BETWEEN THE CARRIER AND THE SOLUTION

A simple behaviour may be observed in the electrostatic interaction between the substrate and the carrier. Indeed, if the carrier and substrate are both charged, the substrate concentration C_0' on (or in) the carrier is defined by the following relation:

$$P = \frac{C_0'}{C_0} = \exp\left(-\frac{ze\psi}{kT}\right), \qquad (46)$$

analogous to Eqn. (43), where P is the partition coefficient, C_0 the substrate concentration in the solution, and ze the charge of the substrate. Then the rate of the reaction in the carrier phase catalysed by the immobilised enzyme can be represented by Eqn. (19), in which the physical significance of the coefficient P is defined by Eqn. (46). Consequently the effective Michaelis constant observed experimentally is given by the relation $K_{m(obs)} = K_m' \exp(ze\psi/kT)$. Evidently, when the charges of the carrier and the substrate are of the same sign (ze and ψ are of the same sign), $K_{m(obs)} > K_m'$; on the other hand, when they are of different sign (ze and ψ are of different signs), $K_{m(obs)} < K_m'$§. It follows from Eqn. (19) that the electrostatic interaction between the substrate and the carrier is not manifested when $C_0 \gg K_{m(obs)}$.

Table 8. The observed Michaelis constants for different immobilised enzymes[7].

Enzyme	Carrier	Charge of carrier	Substrate	Charge of substrate	$K_{m(obs)}$, M	Refs.
ATP : creatine phosphotransferase	None		ATP	−	6.5×10^{-4}	
	p-Aminobenzylcellulose	0	ATP	−	8.0×10^{-4}	127
	KM-Cellulose	−	ATP	−	7.0×10^{-3}	
Ficin	None		EEBA[a]	+	2.0×10^{-2}	
	KM-Cellulose	−	EEBA	+	2.0×10^{-3}	122
Trypsin	None		BAA[b]	+	6.8×10^{-3}	
	Ethylene–maleic acid copolymer	−	BAA	+	2.0×10^{-4}	113
Papain	None		EEBA	+	1.9×10^{-2}	
	pp-Aminophenylanaline-L-leucine copolymer	0	EEBA	+	1.9×10^{-2}	128
Bromelain	None		EEBA	+	0.11	
	KM-Cellulose	−	EEBA	+	0.049	129

[a] EEBA = ethyl ester of *N*-benzoyl-L-arginine.

[b] BAA = *N*-benzoyl-L-argininamide.

§ One should note that there is an error in the fundamental communication of Goldstein et al.[113], which was unfortunately subsequently transferred to other papers by the same workers and also to certain reviews[8,9]. After deriving correctly Eqn. (44), the authors[113] then adopt as the pH shift between the medium of the carrier and the solution the observed shift of the pH profile of the catalytic activity of the enzyme, which evidently is of the opposite sign. As a result negatively charged carriers would have to be characterised by a positive potential ψ! On the basis of this erroneous postulate, the authors quote an incorrect equation for the distribution of the charged substrate between the charged carrier and the solution [cf. Eqn. (46)]:

$$C' = C_0 \cdot \exp\left(\frac{ze\psi}{kT}\right).$$

We may note that this error is by no means purely terminological, since the last equation and the equation for the pH shift between the carrier and the solution [Eqn. (44)], quoted by Goldstein et al.[113], are mutually exclusive.

Table 8 presents the values of $K_{m(obs)}$ for certain reactions of charged substrates with enzymes immobilised on the charged carrier. Evidently in many systems the electrostatic interactions between the substrate and the carrier may result in a difference between $K_{m(obs)}$ and K'_m greater than by an order of magnitude. As was to be expected, at high ionic strengths of the solution the above effects become insignificant. Thus $K_m = 6.9 \times 10^{-6}$ M was found for the reaction of trypsin with the ethyl ester of *N*-benzoyl-L-arginine in solution; $K_{m(obs)} = 0.2 \times 10^{-6}$ M at an ionic strength of 0.04 M and $K_{m(obs)} = 5.2 \times 10^{-6}$ M at an ionic strength of 0.50 M for trypsin immobilised on a copolymer of ethylene and maleic acid[113].

The interaction between the substrate and the carrier can in principle be other than electrostatic. In the general case, when P cannot be predicted theoretically, it can be measured in a separate experiment (using a carrier without the enzyme). For example, in the case of a hydrophobic substrate $P > 1$ may be expected for a hydrophobic carrier and $P < 1$ for a hydrophilic matrix. In the reaction with a hydrophilic substrate the opposite situation may obtain. The nature of the distribution (the value of P) has in turn a corresponding effect on the observed Michaelis constant [Eqn. (19)]. As an example we may point to the reaction of immobilised cholinesterase with benzoylcholine (a hydrophobic substrate), for which the observed Michaelis constant decreases approximately by a factor of ten on passing from a hydrophilic to a hydrophobic matrix[130]. It has been shown[131] that, in the adsorption of lipase on a hydrophobic carrier (siliconised glass), the rate of its reaction with tripropionin [glycerol tripropionate (Ed. of Translation)] increases sharply owing to the concentration of the hydrophobic substrate at the surface of the carrier.

3. DISTRIBUTION OF INHIBITORS AND COFACTORS BETWEEN THE CARRIER AND SOLUTION

When the enzyme reacts with an inhibitor or a cofactor, their influence on the reaction rate is known to be determined[114] by the product $K_G[G]_b$, where $[G]_b$ is the concentration of the inhibitor or the cofactor and K_G is the constant for its binding to the enzyme. For immobilised enzymes, we have the analogous product $K'_G[G]'_b$, where $[G]'_b$ is the concentration of the effector on (or in) the carrier and K'_G is the constant for the binding of the immobilised enzyme to the effector. However, in a kinetic experiment it is possible to find only the effective factor $K_{G(obs)}[G]_b$, where $K_{G(obs)} = K'_G P_G$ and $P_G = [G]'_b/[G]_b$ is the partition coefficient. Evidently all that has been said above about the distribution of the substrate between the carrier and the solution applies to the partition coefficient P_G.

As an example, we may mention β-fructofuranosidase immobilised on polyaminostyrene (a hydrophobic carrier), where the observed constant for inhibition by aniline is higher by a factor of three compared with the reaction of the native enzyme[132].

IV. THE CHANGE IN THE TRUE KINETIC PARAMETERS OF ENZYMIC REACTIONS AFTER IMMOBILISATION

The true kinetic parameters should be understood as quantities uncomplicated by the influence of diffusion factors or the distribution of the reactants between the carrier phase and the solution. There are at least two main causes responsible for the change in the true kinetic parameters after immobilisation. Firstly, the immobilised enzyme can have a conformation different from that of the native enzyme. This type of explanation can be frequently encountered in the literature. However, in practice it can be neither confirmed nor disproved experimentally. There are at present no reliable experimental data indicating the existence of effects of this kind. The second cause is a possible change in the medium in which the enzymic reaction takes place after immobilisation. In certain instances the effect of the medium on the enzymic process can be satisfactorily accounted for within the framework of the influence of the dielectric constant on the ionic strength, particularly for reactions between charged species[133,134].

According to Laurent's concept[135], when neutral polymers are introduced into the solution the chemical potentials of the macromolecules in it change owing to their exclusion from part of the volume of the solvent. Theoretical analysis (which was confirmed experimentally) showed that this phenomenon can lead to the decrease of the observed Michaelis constant (or of the observed constant for the inhibition by the protein). Possibly similar phenomena occur also when enzymes are immobilised.

V. STERIC RATE LIMITATION IN REACTIONS OF IMMOBILISED ENZYMES WITH MACROMOLECULAR SUBSTRATES

Immobilised enzymes (particularly in porous carriers) as a rule retain a high catalytic activity with respect to low-molecular-weight substrates but in many cases lose at the same time the capacity to catalyse reactions involving high-molecular-weight compounds. Thus it has been found[136] that trypsin immobilised in silica gel reacts with the ethyl ester of *N*-benzoyl-L-arginine almost like the native enzyme but does not hydrolyse casein at all. Water-insoluble derivatives of polytyrosyltrypsin and polytyrosylpapain[138] cleave casein at rates amounting to only 15 or 30% respectively of the values which might have been expected on the basis of their intrinsic activities with respect to the low-molecular-weight substrate. Similar results were obtained also for KM-cellulose derivatives of ficin[43,122], bromelain[139], trypsin[140], α-chymotrypsin[137,140], and also for polyalcohol, polyanionic, and polycationic derivatives of papain[8] and subtilopeptidase A.[9] In all these cases the decrease of protolytic activity is probably related to steric hindrance of the approach of the protein substrate to the immobilised enzyme[13,14,17,137]. The same steric factors are also responsible for another finding, namely that immobilised trypsin is 92% inhibited by the comparatively low-molecular-weight pancreatic protein trypsin inhibitor and is not inhibited at all by the more bulky soya bean inhibitor[141].

Certain quantitative relations have been traced[142]. Suppose that χ is the specific activity of pronase immobilised on a water-insoluble copolymer of *p*-aminophenylalanine and leucine, referred to the specific activity of the native enzyme. It was found that $\chi^{1/3}$ varies linearly with $M^{1/2}$, where M is the molecular weight of the substrate. The authors[142] drew attention therefore to data[143,144] for the distribution of various proteins between the aqueous solution and Sephadex. It was shown for this system that not all the solvent which has diffused into Sephadex is accessible to proteins and that only a fraction $N < 1$ is

available, the relation between N and M being satisfactorily described by the equation

$$\sqrt[3]{N} = \text{const}_1 - \text{const}_2 \cdot \sqrt{M} \quad . \qquad (47)$$

Therefore the authors[140] suggest that in the immobilised enzyme system which they describe a similar effect may occur, i.e. only a fraction of the volume of the porous particle containing the immobilised enzyme is accessible to protein substrates, its value depending on M in the way indicated by Eqn. (47).

Steric hindrance in reactions with immobilised enzymes may be combined with electrostatic interaction between high-molecular-weight substrates and the charged carrier. Trypsin immobilised on an anionic carrier cleaves only ten peptide bonds in pepsinogen (and also in reduced carboxymethylated pepsinogen), while the native enzyme cleaves fifteen such bonds[145]. The same trypsin derivative cleaves myosin approximately fifty times more slowly than the native enzyme and at different peptide bonds[146,147]. Native deoxyribonuclease and the enzyme immobilised on glass cleave DNA into different oligonucleotides[148]. Similar effects were also noted in other studies[149-151].

Summarising, one may conclude on the basis of the data presented in Sections III–V that the substrate specificity of the immobilised enzyme can depend strongly on the nature of the carrier and hence may differ significantly from the specificity of the native biocatalyst.

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Only some kinetic and thermodynamic features of catalysis by immobilised enzymes have been explained in the present review from physicochemical standpoints. Many problems remain outside the present discussion. This is because there is so far no quantitative theory in many fields of study involving catalysis by immobilised enzymes. The most important of these are as follows.

1. The study of the dependence of the catalytic activity and substrate specificity of immobilised enzymes on the nature of the carrier (particularly in relation to the individual stages of enzymic catalysis). It is necessary to set up criteria for the choice of the optimal carrier for the given enzyme system.
2. The explanation of the causes of the stabilisation of enzymes on immobilisation. Only the first steps have been taken in this field[152].
3. The development of methods for the immobilisation of enzymes with cofactors and of polyenzyme systems.
4. More attention should be paid in terms of technology to the possibility of the application of "naturally" immobilised systems, in particular micro-organisms.
5. Problems associated with the choice of the optimal reactor for the given process.

In studies on immobilised enzymes efforts should be concentrated on the solution of the above problems.

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Energy Transfer Between Organic Molecules and Transition Metal Ions

V.L.Ermolaev, E.G.Sveshnikova, and T.A.Shakhverdov

Modern ideas on radiationless energy transfer in solutions are described briefly. The fundamental formulae for the rates of this process, involving inductive-resonance and exchange-resonance mechanisms, are presented. Studies on the quenching of the fluorescent and triplet states of organic molecules by transition metal ions are surveyed and it is shown that in most cases radiationless energy transfer takes place.

Energy transfer from a fluorescent state to transition metal ions proceeds via a dipole-dipole mechanism and energy transfer from a triplet state involves an exchange-resonance mechanism. Studies on radiationless energy transfer between transition metal ions and molecular oxygen are also considered. The prospects for using energy transfer to elucidate the pathways and mechanisms of photochemical reactions of coordinated transition metal compounds in solutions are discussed.

The bibliography includes 110 references.

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I. MODERN IDEAS ABOUT THE MECHANISMS OF THE RADIATIONLESS TRANSFER OF ELECTRONIC EXCITATION ENERGY

In the last decade electronic energy transfer has found increasing applications in the solution of chemical, physical, and biological problems [1-6]. The method of triplet–triplet energy transfer between organic molecules, which is nowadays used in every other study on the mechanisms of photochemical reactions, constitutes the most striking example [1-4].

It has become evident in the last five years [7-9] that there exists yet another large chemical field where the application of energy transfer is extremely promising, namely the coordination chemistry of transition metal ions and lanthanide ions in solution. Radiationless energy transfer methods yield much information about the kinetics and mechanisms of the formation of complexes and photochemical reactions involving coordination compounds. In the present review attention is concentrated on the possibilities arising from the application of energy transfer in the study of interaction between transition metal ions and organic molecules in solution.

The radiationless transfer of electronic excitation energy in solution has been most thoroughly investigated for the interaction between two organic molecules [10,11]. The study of energy transfer from organic molecules to transition metal ions began only in the last few years. Since a review dealing with this field has not so far been published, the present survey is submitted to the reader.

Energy transfer in solution frequently proceeds via one of two fundamental mechanisms: inductive-resonance or exchange-resonance. In the inductive-resonance mechanism the interaction of an excited energy donor species with an unexcited acceptor species takes place via electromagnetic fields. Only interactions between electric dipole transitions in the donor and acceptor (dipole–dipole energy transfer) have so far been observed experimentally in solution. The theory of this type of energy transfer has been fairly thoroughly developed by Förster [10] and Galanin [11]. The expression defining the rate constant for energy transfer by this mechanism between a donor and an acceptor at a distance R is [12]

$$k_n(dd) = 8.8 \cdot 10^{-25} n^{-4} \tau_{0D}^{-1} q_{0D} R^{-6} \Phi^2 \int I_D^n(\nu)\, \varepsilon_A(\nu)\, \nu^{-4}\, d\nu \ (\text{in } s^{-1}), \quad (1)$$

where n is the refractive index of the solution, τ_{0D} and q_{0D} are the decay time and the luminescence quantum yield of the donor in the absence of the acceptor, Φ^2 is a coefficient which depends on the orientation of the dipole moments of the transitions in the donor and the acceptor ($\Phi = \cos\varphi_{D^*A} - 3\cos\varphi_{D^*}\cos\varphi_{A}$), [12-14] $I_D^n(\nu)$ the quantum intensity distribution in the luminescence spectrum of the donor normalised for a unit surface area, $\epsilon_A(\nu)$ the molar decadic extinction coefficient of the acceptor, and ν the wavenumber (cm^{-1}).

The expression for the critical radius of energy transfer (R_0) corresponding to the distance over which energy transfer and intramolecular deactivation are equally probable [i.e. $k_t(R_0) = \tau_{0D}^{-1}$] is:

$$R_0^6 = 8.8 \cdot 10^{-25} n^{-4} q_{0D} \Phi^2 \int I_D^n(\nu) \varepsilon_A(\nu) \nu^{-4} d\nu \ . \quad (2)$$

In the presence of sufficiently rapid molecular rotation the average value $\bar{\Phi} = \sqrt{2}/3$ in the calculation of R_0 for solid solutions by Eqn. (2) becomes $\bar{\Phi} = 0.845 \times \sqrt{2}/3$. [13,14] The phenomenon of singlet–singlet energy transfer between organic molecules, which has been thoroughly investigated, constitutes a typical example of dipole–dipole interaction [15].

The exchange-resonance mechanism of energy transfer becomes of primary importance when the radiative transitions in the donor and acceptor are forbidden by selection rules. Its occurrence requires an overlap of the electron clouds of the energy donor and acceptor. The formula describing the rate of transfer via the exchange-resonance mechanism is [16]

$$k_t(ex) = \frac{2\pi}{\hbar} Y \cdot e^{-\frac{2R}{L}} \int I_D^n(\nu)\, \varepsilon_A^n(\nu)\, d\nu \ , \quad (3)$$

where Y is a constant which cannot be determined from optical experiments, L is the average effective Bohr radius

characterising the rate of decrease of electron density in the peripherial regions of the interacting molecules (ions) of the energy donors and acceptors, and $I_D^n(\nu)$ and $\epsilon_D^n(\nu)$ are the emission spectrum of the donor and the absorption spectrum of the acceptor normalised for a unit surface area. The constant $k_t(ex)$ is also directly proportional in this case to the overlap integral of the normalised spectra and decreases exponentially with the distance between the donor and the acceptor. The exchange-resonance interactions are responsible for the triplet–triplet energy transfer between organic molecules [17].

Formulae for the laws governing the interaction in energy transfer via dipole–dipole (*dd*) and exchange-resonance (*ex*) mechanisms between individual molecules were given above. In a real experiment we do not observe these individual laws but the situation which arises as a result of the averaging of the interaction of unexcited acceptor molecules which have a random distribution in solution relative to the excited energy donor molecules. A number of studies have been devoted to mathematical models of the averaging, starting with those of Förster [10] and Galanin [11].

The following energy transfer parameters in solution are usually observed experimentally: (1) the decrease of the luminescence quantum yield of the energy donor as a function of acceptor concentration C_A: $q_{oD}/q_D = f(C_A)$; (2) the decrease of the average duration of donor luminescence as a function of acceptor concentration: $\bar{\tau}_{oD}/\bar{\tau}_D = f'(C_A)$; (3) the change in the donor luminescence decay law in the presence of the acceptor; (4) the change in these relations when the viscosity, temperature, solvent, and other parameters are varied; (5) the intensity (yield) of sensitised acceptor luminescence as a function of acceptor concentration: $q_{s.a.l.} = f''(C_A)$; (6) the sensitised acceptor luminescence excitation spectra, and many other parameters.

The concentration $(C_A)_e$ for which $q_{oD}/q_D = e$ can be determined from the variation of the degree of quenching of donor luminescence with acceptor concentration in solid (highly viscous) solutions. Hence the experimental critical energy transfer radius can be found† from the formula

$$R_0^{exp} = \frac{7{,}35}{\sqrt[3]{(C_A)_e}} \quad (R_0^{exp} \text{ in Å and } C_A \text{ on molar scale}). \tag{4}$$

Comparison of R_0^{exp} with R_0^{theor} calculated by Eqn. (2) makes it possible to reach a conclusion about the energy transfer mechanism. Another convenient parameter which depends on the transfer mechanism in solid (highly viscous) solutions is the ratio of the slopes of the curves

$$\rho = \lim_{C_A \to \infty} \left[\frac{d(q_D/q_{oD})}{dC_A} \Big/ \frac{d(\bar{\tau}_D/\bar{\tau}_{oD})}{dC_A} \right], \tag{5}$$

which is two for the dipole–dipole transfer, as shown correctly for the first time by Galanin [14]. Later a similar problem for other types of energy transfer was discussed by Sveshnikov and Shirokov [18] and Inokuti and Hirayama [19].

On passing to liquid solutions, it is necessary to take into account the mutual diffusion of donor and acceptor molecules during the lifetime of the excited state of the former. The presence of diffusion increases the degree of quenching of the donor in the presence of a specific concentration of the acceptor, provided that τ_{oD} remains unchanged on passing from a solid to a liquid solution. In the general case of random diffusion, its influence on energy transfer can be taken into account in terms of the theory developed by Rozman and coworkers [20], but only with the aid of computer calculations. An important new parameter in such calculations is the distance R_{min} of closest approach of the excited energy donor and the acceptor. The lack of accurate data for R_{min} may introduce the largest error into the calculations of the parameters of dipole–dipole energy transfer with allowance for diffusion. On the other hand, the marked dependence of energy transfer on R_{min} can yield valuable information about the immediate environment of the interacting species (the energy donor and acceptor). For steady-state excitation, the influence of the diffusion of the donor and acceptor on the energy transfer can be taken into account also by the method which was proposed by Bagdasar'yan and Muler [21]. Their tables make it possible to compare the experimental and theoretical data.

In very fluid (non-viscous) solvents the limiting case of "total mixing" in Galanin's terminology [11] may be attained. Under these conditions, the quenching of donor luminescence remains exponential at all the concentrations of the quenching agent and the decrease of the donor luminescence yield and τ in the presence of the acceptor is the same in each case ($q_{oD}/q_D = \tau_{oD}/\tau_D$) and is a linear function of the acceptor concentration. Tunitskii and Bagdasar'yan [22] showed that the quenching rate constant in this limiting case of "infinite diffusion coefficients" is related by a simple mathematical expression to the critical energy transfer radius and the distance of closest approach:

$$k_t^{theor} = \frac{4}{3}\pi N' \frac{R_0^6}{R_{min}^3} \cdot \frac{1}{\tau_{oD}} \text{ (litre mole}^{-1}\text{ s}^{-1}\text{)}, \tag{6}$$

where $N' = 10^{-3}N$ and N is the Avogadro number. Eqn. (6) is in fact the same as the formula derived earlier by Galanin and Frank [23] using the classical model for energy transfer from an emitting dipole to a continuous absorbing medium. The condition for the applicability of Eqn. (6) is

$$\sqrt{\gamma'/\sigma} \ll 1, \text{ where } \gamma' = \left(\frac{R_0}{R_{min}}\right)^6; \ \sigma = \frac{D\tau_{oD}}{R_{min}^2},$$

$D = D_D + D_A$ is the sum of the diffusion coefficients of the donor and acceptor.

The exponential quenching of donor luminescence and the linearity of the relation $q_{oD}/q_D = \tau_{oD}/\tau_D = \text{const.} C_A$ are maintained also for $(R_0^2/D\tau_0)^{3/2} \ll 1$; alternatively we have approximately $\bar{r} = \sqrt{2D\tau_{oD}} > R_0$, i.e. when the mean square displacement ($\bar{r}$) during the lifetime of the excited state of the donor exceeds severalfold the critical energy transfer radius R_0. On the other hand, for large values of R_0 the last condition cannot correspond to the case of "total mixing" and Eqn. (6) becomes invalid. A fairly complex mathematical expression for k_t under these conditions was derived by Tunitskii [24]. The $D^{3/4}$ law discovered by Yokota and Tanimoto [25] is a special case when $1 \ll 5(D\tau_{oD}/R_0^2)^3 \ll (D\tau_{oD}/R_{min}^2)^2$. Then k_t^{theor} is also described by the simple expression

$$k_t^{theor} = 2\pi^{3/2} N' D^{3/4} R_0^{3/2} \tau_{oD}^{-1/4}. \tag{7}$$

All the above considerations refer to energy transfer between electrically neutral species. However, in many cases the energy donor and acceptor exist in solution as electrically charged species: anions or cations. Thus the theory of radiationless energy transfer must take into account the electrostatic interactions between the energy donor and acceptor and the deviations caused by them from the random distribution of acceptor species around

† In a dipole–dipole energy transfer the concentration $(C_A)_e$, determined from the change of q_D, corresponds to $(C_A)_2$, i.e. to twofold quenching determined from the decrease of τ_D. [19]

the excited donor. This theory was developed by Bodunov [26-28] in terms of the *dd* approximation for solid and liquid solutions. As a result of the electrostatic interaction between the donor and acceptor, the acceptor concentration as a function of the distance from the donor becomes:

$$C_A(r) = C'_A \cdot \exp(-U(r)/kT),$$

where C'_A is the acceptor concentration far from the excited donor and $U(r)$ the electrostatic interaction energy between ions. It has been assumed [26] that $U(r)$ is determined by shielded Coulombic interaction. In his later studies Bodunov [27,28] found the interaction energy as the exact solution of the Poisson equation for the electrostatic potential generated by D* in an electrically neutral solution.

It was shown in the above studies that the effect of electrostatic interaction on *dd* energy transfer for ions bearing charges of the same sign is significant mainly in liquid solutions alone. In solid solutions the contribution of these interactions does not exceed 10–20% and therefore cannot be detected experimentally. For ions bearing charges of different sign, this influence can be manifested also in the absence of diffusion-controlled processes in the solution. The dependence of energy transfer on the electrostatic interaction between ions is determined by many factors, the main ones of which are the dielectric constant of the solvent ϵ and the distance of closest approach between the ions $R\,\mathrm{min}$ (for ions having different charges). For $C_A > C_D$, electrostatic interactions can lead to a curvature (in consequence of the shielding effect of the acceptor molecules) of the relations between q_{0D}/q_D and C_A. The form of this curvature depends on whether the energy donor and acceptor have the same or different charges. The shielding or suppression of electrostatic interaction can also be achieved by adding extraneous electrolytes to the solution.

The number of studies dealing with the theory of analogous problems in relation to the exchange-resonance type of energy transfer is significantly smaller [19]. It has been shown that in a highly viscous solution the energy donor luminescence quantum yield should decrease much faster than the average decay time of donor luminescence. The experimental discrepancy between the ratios q_{0D}/q_D and $\bar{\tau}_{0D}/\bar{\tau}_D$ makes it possible to estimate the average effective Bohr radius L in Eqn.(3).[19] In liquid solutions the exchange-resonance energy transfer obeys in most cases the same relations as other "fast" chemical reactions involving excited species, for example electron transfer reactions and other collision-controlled processes [29,30].

Thus the determination of the rate constants for energy transfer reactions, the ratio of the decrease of the donor luminescence yield to τ, the law governing the decay of donor luminescence in the presence of an acceptor, and the variation of the energy transfer characteristics with the concentrations of the components, the solvent, and the spectral characteristics of the interacting species makes it possible to establish the mechanism of the energy transfer in each specific case. In many instances it is possible to obtain information from energy transfer data about the existence of short-lived unstable complexes, which cannot be detected by other methods.

Below we shall attempt to arrange systematically experimental data which throw light on the mechanism of the interaction in the quenching by transition metal ions of the excited singlet and triplet states of organic molecules and of singlet oxygen. Data concerning the influence of the structure of these molecules and complexes and also of the solvent on the quenching rate constants will be considered. In addition, we shall discuss the applications of energy transfer in the study of the mechanisms of photochemical reactions of transition metal complexes of different types.

II. THE MECHANISM OF THE QUENCHING OF THE FLUORESCENCE OF ORGANIC COMPOUNDS BY TRANSITION METAL IONS

The quenching of the fluorescence of organic compounds by transition metal ions in solution has been known for a long time [31,32], but its mechanism still remains not altogether clear. Weiss [33] rejected the idea that such quenching is related to the intersystem crossing catalysed by the paramagnetism of the quenching agents on the grounds that many paramagnetic ions (for example Mn^{2+}) do not quench the fluorescence of dyes. Linschitz and Pekkarinen [34] also observed only very weak quenching effects due to Mn^{2+} and Zn^{2+} ions. To explain the quenching of the fluorescence of organic molecules by transition metal ions, Terenin [35] and later Linschitz and Pekkarinen [34] proposed a reversible charge transfer mechanism. The latter workers [34] noted a parallelism between the quenching efficiencies for fluorescence and for the triplet state [34,36-38]. However, sufficiently convincing experimental results establishing a relation between the degree of quenching and the redox potentials of the cations were not quoted.

Another concept was put forward by Galanin and Lëvshin [39]. They attributed the pronounced quenching of the fluorescence of quinine sulphate and 3-aminophthalimide by Cr^{3+} in glycerol to inductive-resonance energy transfer from these organic molecules to Cr^{3+}. There is at present a growing interest in the mechanism of the processes involved in the quenching of the fluorescence of organic compounds by transition metal ions. This is related mainly to the recent observation of the sensitising action of organic molecules on photochemical reactions of transition metal complexes. Naphthalene sensitises the photochemical reduction of $[Co(NH_3)_6]^{3+}$ to Co^{2+}.[40] The Stern–Volmer fluorescence quenching (200 litre mole^{-1}) and sensitisation (170 litre mole^{-1}) constants proved to be closely similar in this instance. The quinolinium ion also sensitises this reaction [41] via the excited triplet state (k_T = 36.6 litre mole^{-1}). In the sensitised photochemical reduction of $[Co(Phen)_3]^{3+}$ the fluorescence of free *o*-phenanthroline (Phen) is quenched by the complex [42] with k_T = 600 litre mole^{-1}. The sensitised photochemical aquation of the complex $[Cr(NH_3)_5X]^{2+}$, where $X^- = Cl^-$ or NCS^-, i.e. $[Cr(NH_3)_5X]^{2+} \rightarrow [Cr(NH_3)_4(H_2O)X]^{2+} + NH_3$, has been investigated in solutions containing acridinium ions [43] and riboflavine [44]. The simultaneous quenching of the fluorescence of the latter was observed. The fluorescence of naphthalene is quenched when it sensitises the photochemical reaction of $[Cr(CN)_6]^{3-}$.[45]

Varnes et al.[46] studied the effect of 13 metal ions on the fluorescence of riboflavine. The decrease of the fluorescence yield on quenching is consistent with the decrease of its τ and obeys a linear relation. With increase of temperature, k_T rises, while an increase in viscosity causes its diminution. However, the results obtained do not yield clear-cut conclusions concerning the mechanism of the quenching of fluorescence.

We attempted to revise the above data [40,43,44,46] as well as the results of earlier studies by Weber [47,48] from the standpoint of energy transfer via the dipole (*dd*) mechanism. Table 1 presents the experimental k_T from the

above studies, and our calculated overlap integrals of the spectra (J_O), the critical energy transfer radii (R_0^{theor}), and the theoretical energy transfer rate constants (k_t^{theor}). The k_t^{theor} were calculated by Eqn. (6) assuming infinite diffusion coefficients and $R_{min} = 8$ Å.

Table 1. The quenching of the fluorescence of organic compounds by transition metal ions.

Donor	Transition metal ion	$10^{-9}k_q$, litre mole^{-1} s^{-1}	$10^{-17}\times\int\varepsilon_A$	$10^{26}k_q/J_O$	R_0, Å	$10^{-9}k_t^{theor}$ litre mole^{-1} s^{-1}
Naphthalene* (H_2O + EtOH (1:1); 293 K $\tau_{fl}^0 \cong 1$ ns, $q_{fl}^0 \cong 10^{-1}$] (Ref.40)	$[Co(NH_3)_4]^{3+}$	~20	5,1	—	10	~5 ~12 (R_{min}=6Å)
Acridinium ion (H_2O + 0.1 *N* H_2SO_4; 298 K τ_{fl}^0 = 43 ns, q_{fl}^0 = 0.77) (Ref.43)	$[Cr(NH_3)_5NCS]^{2+}$	6.0	32	—	18,9	5,3
Riboflavine (H_2O, pH 3.2; 298 K)(Ref.44)	$[Cr(NH_3)_5NCS]^{2+}$	4,2	17	0,25	14,1	6,2
	$[Cr(NH_3)_5Cl]^{2+}$	5.2	18	0,29	14,3	6,7
Riboflavine (H_2O, pH 2.6; 303 K: τ_{fl}^0 = 4.7 ns; q_{fl}^0 = 0.75) (Ref.46)	V^{3+}	4,6	3,7	1,2	11,0	1,8
	Cr^{3+}	3,6	8,4	0,4	12,6	3,6
	Co^{2+}	3,2	1,7	1,9	9,6	0,83
	Cu^{2+}	1,2	0,32	3,8	7,3	0,16
	Ni^{2+}	0,55	0,24	2,3	6,9	0,12
	Mn^{2+}	<0,04	0,03	<1,3	4,9	0,015
	Zn^{2+}, Ba^{2+}, Pb^{2+}	<0,04	0,00	—	—	—
	Fe^{2+}	3,6	0,08	45	—	—
Quinine sulphate** (H_2O + 1 *N* H_2SO_4; 293 K; $\tau_{fl}^0 \cong 20.1$ ns, q_{fl}^0 = 0.54) (Refs.47,48)	Cr^{3+}	7,5	3,8	2,0	12,5	0,94
	Co^{2+}	2,3	1,8	1,3	11,1	0,45
	VO^{2+}	0,50	0,68	0,7	9,4	0,17
	Ni^{2+}	0,26	0,54	0,5	9,0	0,13
	Cu^{2+}	0,17	0,13	1,3	7,1	0,032
	Mn^{2+}	0,023	0,01	2,3	4,8	0,003
	Fe^{2+}	1,3	0,02	650	—	—

*τ_{fl}^0 and q_{fl}^0 were estimated by the present authors.
**The values of k_q for this compound were estimated by the present authors from the literature data [47,48] on the assumption that the Stern–Volmer relation between q_0/q and C_A holds and that $\tau_{fl}^0 \simeq 20.1$ ns.

We established that the error for $\sigma/\gamma' > 1.5$ arising from the use of this formula does not exceed 10% of the overall error. For systems comprising riboflavine and $[Cr(NH_3)_5X]^{2+}$ (with $X^- = NCS^-$ or Cl^-), $[Cr(H_2O)_6]^{3+}$, and $[V(H_2O)_6]^{3+}$, where $\sigma/\gamma' < 1.5$, calculations of k_t^{theor} were made on a computer by the method of Rozman and coworkers [49] using $D \simeq 1 \times 10^{-5}$ cm^2 s^{-1}.

Examination of the data in Table 1 leads to the following conclusions: (1) in most cases there is a satisfactory correlation between k_q and J_O (except for the Fe^{2+} ion); (2) the experimental quenching rate constants (k_q) are appreciably greater (by a factor of 2–8) than the calculated rate constants for energy transfer via the *dd* mechanism (k_t^{theor}).

In many instances the differences between the above quantities are small and can be entirely due to the inaccuracy of the parameter R_{min}. If the energy donor is charged, one must also consider the influence of the electrostatic interaction of the ions on the fluorescence quenching process.

Thus the parallel variation of k_q and overlap integrals of the spectra and the agreement within an order of magnitude between k_q^{exp} and k_t^{theor}, estimated from the formulae for *dd* energy transfer, demonstrate convincingly that the radiationless energy transfer from excited singlet states of organic compounds to transition metal ions is one of the most likely processes responsible for quenching when the fluorescence spectra overlap with the absorption spectra of transition metal ions.

The marked discrepancy between k_q^{exp} and k_t^{theor} for Fe^{2+} is probably due to the fact that the reversible electron transfer to the excited molecule of the organic compound with formation of Fe^{3+} via Terenin's mechanism [35] is dominant under these conditions.

III. THE MECHANISM OF ENERGY TRANSFER FROM TRIPLET STATES OF ORGANIC MOLECULES TO TRANSITION METAL IONS

1. SOLID SOLUTIONS

The mechanism of the quenching of the phosphorescence of organic compounds by transition metal ions has also been inadequately elucidated. In the first studies by Pankeeva [50,51], carried out in solid solutions of ethanol and acetic and formic acid at 90 K, it was postulated that the transition metal ions exhibit a paramagnetic effect on the phosphorescence, i.e. they initiate a radiationless intercombination transition from the triplet to the ground state. She studied the quenching of the phosphorescence of fluorescein and trypaflavine by Ni^{2+}, Mn^{2+}, and Fe^{3+} ions and found that the relations between q_D/q_{oD} and τ_D/τ_{oD} on the one hand and the transition metal concentration on the other differ markedly and the two ratios vary exponentially with the concentration of quenching agents. Smaller et al. [52] studied by ESR the quenching of the phosphorescence of perdeuteronaphthalene (naphthalene-d_8) in a 9:1 mixture of methanol and water at 77 K by Cu^{2+}, Ni^{2+}, Co^{2+}, Mn^{2+}, Fe^{3+}, and Gd^{3+} ions. They discovered a non-rigorous proportionality between the rate of such quenching and the magnetic moments (in Bohr magnetons) of the transition metal ions, which they regarded as supporting a mechanism of paramagnetic influence of the quenching agents (for a criticism of this study, see below).

Hill and Lin [53,54] used Hoijtink's idea [55,56] about the involvement of exchange interactions in the postulated quenching of the triplet state of organic molecules catalysed by paramagnetic transition metal ions. They compared the experimental parameters of the quenching of the naphthalene-d_8 phosphorescence in ethanol by Co^{2+}, Cr^{3+}, Cu^{2+}, and Ni^{2+} ions (at 77 K) with the theoretical values calculated on the basis of the above model. They were the first to note the non-exponential quenching of the phosphorescence in the presence of paramagnetic substances in addition to the discrepancy between the variations of q_D/q_{oD} and τ_D/τ_{oD} with the concentration of such substances.

Best agreement between theory and experiment was achieved for the parameters γ and C_A^0 quoted in Table 2. The diamagnetic Zn^{2+} ion does not quench the phosphorescence up to $C = 0.25$ M. The experimental data [53,54] do not confirm the exchange mechanism for the interaction of naphthalene with transition metal ions. Thus there are considerable variations in C_A^0 in the series of these ions; it is unlikely that the overlapping of electron clouds of

different transition metal ions and naphthalene-d_8 varies quite so much. The values of R_0^{exp} for the above systems are large, i.e. they exceed considerably the sum of the radii of both components. Table 2 also presents the ratios ρ of the limiting slopes of the degree of quenching–concentration curves, which were calculated by Eqn.(5) from determinations [53,54] of the changes in q_{0D} and τ_{0D}. The Table shows that the ratios are in the range 0.50 to 0.57, i.e. are a characteristic of the dipole–dipole energy transfer.

Table 2. The quenching of the phosphorescence of organic compounds by aquated transition metal ions in solution at 77 K.

Donor	Transition metal ions	R_0^{exp*}, A	ρ	C_A^0, M	ν
Naphthalene-d_8 in 95% ethanol (Refs.53,54)	Co^{2+}	12.4	0.50	0.210	4.4
	Cr^{3+}	24.3	~0.55	0.028	10.0
	Cu^{2+}	17.8	~0.50	0.072	12.0
	Ni^{2+}	11.0	0.57	0.298	7.0
Naphthalene-d_8 in 9:1 methanol–water mixture (Ref.57)	Co^{2+}	14.3**	0.52		
	Ni^{2+}	13.4	0.24		
	Mn^{2+}	14.6	0.13		
Triphenylene in 9:1 methanol–water mixture (Ref.57)	Co^{2+}	15.5**	0.50		
	Ni^{2+}	14.4	0.12		
	Mn^{2+}	14.9	0.10		

*The values of R_0^{exp} were obtained [53,54] on the assumption of an exchange interaction and from the condition of best agreement between the experimental and theoretical values of C_A^0. In another study [57] the R_0^{exp} were obtained from the exponential relations between q_D/q_{0D} and C_A within the framework of the model postulating a limited sphere of quenching action.

**On the assumption of dipole–dipole interaction.

The most clear-cut data were obtained in a recent study by Breuninger and Weller [57], who investigated the quenching of the phosphorescence of triphenylene and naphthalene-d_8 by Co^{2+}, Ni^{2+}, and Mn^{2+} ions. The authors treat the observed quenching of the phosphorescence as a radiationless energy transfer from the triplet states of the molecules with excitation of the transition metal ions. The parameters ρ discussed above [see Eqn.(5)] were calculated in the same study [57] (Table 2). $\rho = 0.50-0.52$ for Co^{2+}, which supports the dipole–dipole mechanism of the interaction. For the remaining ions, the parameter ρ is much smaller (about 0.1–0.2) and much closer to the values for exchange interaction [19]. In the naphthalene-d_8–Ni^{2+} system ($\rho = 0.24$) both types of interaction are postulated. Table 2 also lists the values of R_0^{exp}, which exceed somewhat the R_0 for the triplet–triplet energy transfer [17]. The latter finding is incomprehensible. The reason for the small difference between the R_0^{exp} for the dipole–dipole (transfer to Co^{2+}) and exchange (Mn^{2+}, Ni^{2+}) transfer mechanisms deduced from the parameters ρ is also obscure.

Breuninger and Weller [57] showed that the reduction of the intensity of the ESR signal of the naphthalene-d_8 triplet state by paramagnetic transition metal ions, observed by Smaller et al. [26], is due to the broadening of the ESR lines in the presence of the paramagnetic ions, which increases with the magnetic moment of the ion.

2. LIQUID SOLUTIONS

The quenching of the fluorescence of organic molecules in the triplet state by transition metal ions in liquid solutions was observed in 1958 simultaneously by Porter and Wright [37,38] and by Linschitz and Sarkaninen [36]. In the first investigations [36–38] it was suggested that the quenching is due to the radiationless transition of organic molecules to the ground state catalysed by paramagnetic transition metal ions in accordance with the scheme

$$^3D + {}^nM_j^{k+} \rightarrow {}^1D + {}^nM_j^{k+}, \quad n \geqslant 2 \tag{8}$$

or due to reversible electron transfer reactions:

$$^3D + {}^nM_j^{k+} \rightarrow {}^2D^+ + {}^mM_i^{(k-1)+}, \tag{9a}$$

$$^3D + {}^nM_j^{k+} \rightarrow {}^2D^- + {}^mM_i^{(k+1)+}, \tag{9b}$$

where ^3D is the organic molecule in the triplet state, $^2D^+$ and $^2D^-$ are the radical-cation and radical-anion derived from this molecule, and $^nM_j^{k+}$ is the transition metal ion.

Below we shall attempt to show that the most effective process involved in the quenching of triplet molecules of organic compounds by transition metal ions in liquid and solid solutions is radiationless energy transfer. Most of the studies published on this problem in recent years tend to support this view [58–62]. It is noteworthy that the quenching of the triplet state by transition metal ions in solutions is more closely related to chemical interactions than the quenching of fluorescence. The exchange-resonance mechanism of the process responsible for the "physical" quenching in this case requires the overlapping of the electron clouds of the interacting molecules, which is necessary also for the formation of chemical bonds. However, there is no doubt that the existing relation between complex formation and the quenching of triplet molecules by a transition metal ion has so far been traced less distinctly than in the quenching by lanthanide ions [7–9]. Possibly this is related to the lack of systematic studies on this problem.

a. Direct Evidence for Energy Transfer

The sensitised luminescence of transition metal ions,

$$^3D^* + {}^nM_j^{k+} \xrightarrow{k_t} {}^1D + ({}^mM_i^{k+})^*,$$

$$({}^mM_i^{k+})^* \overset{k_R}{\rightsquigarrow} ({}^lM_k^{k+})^* \xrightarrow{k_{em}} {}^nM_j^{k+} + h\nu_{s.l.}, \tag{10}$$

where $^nM_j^{k+}$, $(^mM_i^{k+})^*$, and $(^lM_k^{k+})^*$ is the complex of the transition metal ion in the non-excited, excited Franck–Condon, and excited resonance states from which emission takes place, constitutes direct evidence for radiationless energy transfer between the triplet molecule and transition metal ions. The sensitised luminescence of transition metal ions was observed experimentally for the first time by Binet et al. [58] They observed the simultaneous quenching of the phosphorescence of benzil‡ and the appearance of the sensitised phosphorescence of the complexes $[Cr(NCS)_6]^{3-}$ and $[Cr(CN)_6]^{3-}$ in a deoxygenated mixture of methanol and water at 160 K (Table 3). Anthracene ($^3\Gamma = 14\,950$ cm^{-1}) also sensitises the phosphorescence of chromium(III) complexes at 160 K in the above mixture [58] and at room temperature in dimethylformamide

‡ The fluorescence of benzil is not appreciably quenched under the experimental conditions by complex chromium(III) ions.

(DMF) [59]§. On freezing the solutions, the quenching and intensity of the sensitised phosphorescence were sharply reduced. The rate constants for energy transfer (k_t) estimated from the decrease of the benzil phosphorescence yield, the decrease of its phosphorescence decay time, and the increase in the intensity of the sensitised phosphorescence of chromium(III) complexes with increase of their concentration are listed in Table 3. Their scatter is small, except for $[Cr(NCS)_6]^{3-}$, where the differences are appreciable. It has been suggested [58] that the maximum value of k_t is close to the rate constant for the diffusion of the solvent under the experimental conditions, although viscosity measurements were not made.

Table 3. The rate constants for energy transfer from triplet benzil molecules ($^3\Gamma$ = 18 800 cm^{-1}, τ_0 = 1.5 ms) to chromium(III) complexes in an 88 : 12 methanol–water mixture at 160°C in the absence of molecular oxygen [58].

Acceptor	$10^{-6}k_t$, litre mole^{-1} s^{-1}	^2E_g, cm^{-1}	$^4T_{2g}$, cm^{-1}
$[Cr(NCS)_6]^{3-}$	5÷18	12 900	17 800
$[Cr(acac)_3]$	10	12 800	18 400
$[Cr(urea)_6]^{3+}$	2.8	14 240	16 300
$[Cr(CN)_6]^{3-}$	1.2÷4.0	12 500	26 700
$[Cr(en)_3]^{3+}$	1.3±0.3	15 000	21 900

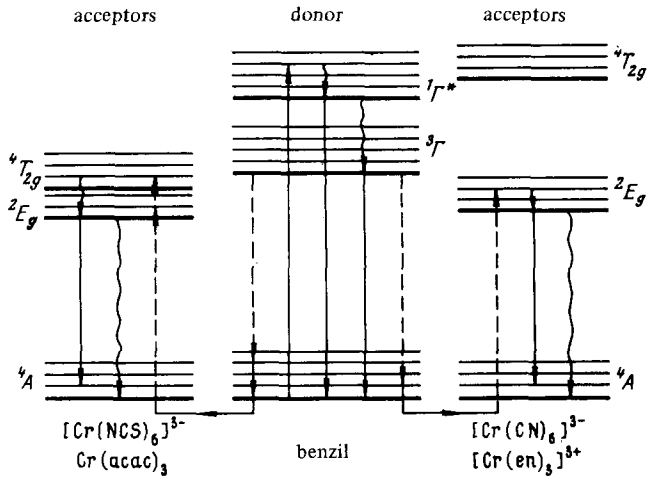


Figure 1. Schematic illustration of the electronic levels in energy transfer from organic molecules (benzil) in the triplet state ($^3\Gamma$) to chromium(III) ions.

If the complex with urea is excluded, then the following observation may be made for the remaining chromium(III) complexes listed in Table 3. The constant k_t decreases abruptly severalfold on passing from complexes where energy transfer to the ^2E_g and $^4T_{2g}$ levels is possible to complexes where energy may be transferred from the benzil triplet level only to the ^2E_g level of Cr^{3+} (Fig. 1).

§ Recently Balzani et al. [60] observed the phosphorescence of $[Cr(en)_3]^{3+}$ sensitised by diacetyl in water at 288 K.

Later Ohno and Kato [61] observed the phosphorescence of chromium(III) complexes sensitised by benzil and erythrosine. They noted that chromium(III) complexes quench effectively the phosphorescence of erythrosine but not its fluorescence. The admission of oxygen does not affect the phosphorescence of Cr^{3+} on direct excitation but fully suppresses its sensitised luminescence. The rate constants for energy transfer from erythrosine to chromium(III) complexes are listed in Table 4. Ohno and Kato [61] attribute the differences between the constants k_t to the aromatic or nonaromatic nature of the ligands in the complexes. However, we believe that the data in Table 4 clearly demonstrate a dependence of k_t on the charge of the complex ion: the higher the negative charge of the complex the smaller the value of k_t¶. This can be understood, since the energy donor (erythrosine) is in all probability present in solution as the dianion.

Table 4. The rate constants for the quenching of the triplet state of erythrosine ($^3\Gamma \simeq$ 14 800 cm^{-1}) in 9 : 1 ethanol–water mixture at 201 K in the absence of molecular oxygen [61].

Acceptor	$10^{-6}k_t$, litre mole^{-1} s^{-1}	^2E_g, cm^{-1}	$^4T_{2g}$, cm^{-1}	$^3\Gamma_{lig}$, cm^{-1}
Cr(oxine)$_3$	48	~13 100		~16 000
Cr(acac)$_3$	12	12 800	18 400	25 400
$[Cr(NCS)_4(aniline)_2]^-$	12	~13 100		~25 000
$[Cr(NCS)_4(NH_3)_2]^-$	6.2	13 300		>25 000
$[Cr(NCS)_6]^{3-}$	1.6	12 900	17 800	>25 000

Ohno and Kato's claim [61] that the constant k_t for energy transfer from erythrosine to [Cr(oxine)$_3$] is equal to the diffusion constant is not altogether correct. The transfer from the excited triplet state of the ligand is indeed endothermic in this case (Table 4)†, but the rate of the triplet–triplet energy transfer is then usually lower than the diffusion rate [63].

A second fairly direct piece of evidence showing that the transfer of electronic excitation energy is in fact usually responsible for the quenching of the triplet state of organic molecules by transition metal ions is the sharp decrease of the quenching rate constant (k_t) when the lower excited resonance level of the transition metal ion in the complex lies above the triplet level, i.e. the energy transfer becomes endothermic. We were able to select from the literature a fairly large number of examples illustrating this postulate. They are presented in Table 5. These data constitute yet another significant confirmation that the quenching of the triplet molecules of organic compounds is caused by radiationless energy transfer.

¶ The chromium(III) and cobalt(III) complexes remain unchanged in solution for a long time, since the rate of exchange of their ligands with the solvent is very low: for example, the rate of thermal exchange between chromium(III) complexes and water is of the order of 10^{-6} s^{-1}. [64]

† The data for the $^3\Gamma$ level of erythrosine listed in Table 1 of Ohno and Kato's paper [61] are erroneous, since they are inconsistent with the Fig. 4 of the same communication and other literature data.

Although the mechanism of the induced catalysis of intersystem crossing in accordance with Eqn.(8), proposed in early investigations [37,38], is in fact possible in the above instances, its probability is lower. Table 5 shows that the rate constants for this process have an upper limit $\leq(0.1-1)\times 10^6$ litre mole^{-1} s^{-1}, which is 1–3 orders of magnitude lower than the rate constants for the energy transfer.

Table 5. The effect of the relative energies of the triplet states of organic molecules and the excited resonance levels of transition metal ions on the rate constants for the quenching of triplet states in solution at 293 K.

Donor	$^3\Gamma_D$, cm^{-1}	Complex*	E_{res}, cm^{-1}	$10^{-6}k_t$, litre mole^{-1} s^{-1}	Solvent	Refs.
Anthracene	14 950	$[Cr(H_2O)_3Cl_3]$	—	200	THF + H_2O	34
ditto	14 950	$[Ni(H_2O)_6]^{2+}$	8 500	160		34
»	14 950	$[Co(H_2O)_6]^{2+}$	8 000	210		34
»	14 950	$[Cu(H_2O)_6]^{2+}$	~9 400	320		34
»	14 950	$[Mn(H_2O)_6]^{2+}$	~19 000	1,3		34
Tetraphenyl-porphin	13 000**	$[Ni(Py)_6]^{2+}$	~8 000—10 000	10	Pyridine	34
	13 000	$[Mn(Py)_6]^{2+}$	18 000—20 000	<0.5		34
Acridine	15 840	$[Cr(C_2O_4)_3]^{3-}$	14 350	610	H_2O	62
ditto	15 840	$[Co(H_2O)_6]^{2+}$	8 000	10		62
»	15 840	$[Cr(OH)_6]^{3-}$	~17 200	<1		62
»	15 840	$[Mn(H_2O)_6]^{2+}$	~19 000	<1		62
Triphenylene	23 500	$[Cr(CN)_6]^{3-}$	12 500	9,7	EtOH + THMF** + H_2O	66
Chrysene	20 000	$[Cr(CN)_6]^{3-}$	12 500	27		66
Anthracene	14 950	$[Cr(CN)_6]^{3-}$	12 500	59		66
Ditto	14 950	$[Cr(en)_3]^{3+}$	15 000	11		66
Naphthacene	10 300	$[Cr(CN)_6]^{3-}$	12 500	<0,2		66

*All the symbols used for the ligands in the complexes here and henceforth are consistent with the generally accepted notation (see, for example, the monograph of Basolo and Pearson [64]).

**According to the data of Gradyushko et al. [65]

***THMF = tetrahydro-2-methylfuran.

An analogy can be drawn with complexes of lanthanide ions. The triplet state of the tris-β-dibenzoylmethanate ($^3\Gamma_{lig} \simeq 20500$ cm^{-1}) of La^{3+} (a diamagnetic ion) has a quenching time $\tau_0 = 0.5$ s for the phosphorescence in an organic glass at 77 K. When La^{3+} is replaced by the paramagnetic Gd^{3+} ion with a high resonance level ($^6P_{7/2} = 32\,000$ cm^{-1}), τ_0 for the ligand decreases to 2×10^{-3} s. [67] On the other hand, τ_0 for the triplet level of the ligand decreases sharply on passing to lanthanide ion complexes with a resonance level below the $^3\Gamma_{lig}$ level of, for example, Eu^{3+} ($^5D_0 \simeq 17\,200$ cm^{-1}) and Sm^{3+} ($^4G_{5/2} \simeq 17\,800$ cm^{-1}). The lifetime of the triplet state of the organic ligand in complexes of this type is shown by the rate of energy transfer to lanthanide ions, to be about 10^{-9} s or less [68,69].

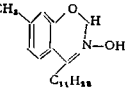
Direct experiments permitting an unambiguous choice between the hypotheses concerning the energy transfer and the catalysis of intercombination transitions as the causes of the quenching of triplet molecules by transition metal ions were described by Allsopp and Wilkinson [70], who showed that the planar diamagnetic nickel(II) and palladium(II) complexes with Schiff bases effectively quench the triplet states of molecules whose triplet level lies above the excited states of transition metal ions in the ligand field (about 2500 cm^{-1} for Ni^{2+} and 16 500 cm^{-1} for Pd^{2+}; see Table 7) but are below the triplet level of the ligand ($^3\Gamma_{lig} \simeq 21\,000$ cm^{-1}). Since the above complexes have a singlet ground state, the possibility of the mechanism involving the spin catalysis of intercombination transitions in accordance with Eqn.(8) is completely ruled out; the only remaining possibility is that these complexes quench via the mechanism involving the heavy atom effect.

Table 6. Effect of the structure of the transition metal complex on the rate of exothermic energy transfer from triplet aromatic hydrocarbon molecules in liquid solutions at 293 K.

Donor	$^3\Gamma$, cm^{-1}	Acceptor	Solvent	$10^{-6}k_t$, s^{-1} litre mole^{-1}	Refs.
Triphenylene	23 500	$[Cr(CN)_6]^{3-}$	H_2O + THMF + EtOH (29:1:70)	9,7	65
ditto	23 500	$[Cr(SCN)_4(NH_3)_2]$		310	65
»	23 500	$[Cr(OC(NH_2)_2)_6]^{3+}$		36	65
Naphthalene	21 250	$[Cr(H_2O)_6]^{3+}$	H_2O	69	34, 38
ditto	21 250	$[Co(H_2O)_6]^{2+}$		50	34, 38
»	21 250	$[Mn(H_2O)_6]^{2+}$		28	34, 38
»	21 250	$[Fe(H_2O)_6]^{3+}$		29	34, 38
»	21 250	$[Cu(H_2O)_6]^{2+}$		75	34, 38
»	21 250	$[Ni(H_2O)_6]^{2+}$		23	34, 38
»	21 250	$[Co(H_2O)_6]^{2+}$		90	34, 38
»	21 250	$[Cr(NH_3)_6]^{3+}$	H_2O+EtOH (1:1)	33	73
»	21 250	$[Cr(NH_3)_5Cl]^{2+}$		200	73
Chrysene	20 000	$[Cr(CN)_6]^{3-}$	H_2O + THMF + EtOH(33:7:60)	27	66
ditto	20 000	$[Cr(en)_3]^{3+}$		62	66
»	20 000	$[Cr(en)_3Cl_2]^+$		200	66
»	20 000	$[Cr(NH_3)_5Cl]^{2+}$		200	66
»	20 000	$[Cr(OC(NH_2)_2)_6]^{3+}$		560	66
»	20 000	$[Cr(SCN)_4(NH_3)_2]^-$		1300	66
Anthracene	14 950	$[Cr(CN)_6]^{3-}$	H_2O+EtOH (3:7)	59	66
ditto	14 950	$[Cr(OC(NH_2)_2)_6]^{3+}$		5,7	66
»	14 950	$[Cr(en)_3]^{3+}$		11	66
»	14 950	$[Cr(NH_3)_5Cl]^{2+}$		30	66
»	14 950	$[Cr(SCN)_4(NH_3)_2]^-$		560	66

Table 7. The rate constants for exothermic energy transfer from triplet molecules to transition metal complexes with aromatic ligands in benzene at room temperature.

Donor	$^3\Gamma$, cm^{-1}	Acceptor	$10^{-9}k_t$, litre mole^{-1} s^{-1}	Refs.
Phenanthrene	21 700	$Fe(acac)_3$	3.3	75
Naphthalene	21 250	$Fe(acac)_3$	1.8	75
Anthracene	14 950	$Fe(acac)_3$	0.7	75
»	14 950	$Cr(acac)_3$	1.3	75
»	14 950	$Cu(acac)_2$	0.6	75
»	14 950	$Cu(dpm)_2$	0.3	75
»	14 950	$Ni^{II}(SB)_2$(planar)	2.6÷4.3	76
»	14 950	$Ni^{II}(SB)_2$(tetr.)	<0.01	76
Chrysene	20 000	Ni^{II}(Hen-Sam-OH)(oct.)	<0.2	76
Benzophenone	24 200	$Fe(dpm)_3$	0.9	77
1-Naphthaldehyde	19 750	$Fe(acac)_3$	2.7	77
	19 750	$Fe(dpm)_3$	0.9	77
2-Acenaphthone	20 800	$Fe(acac)_3$	1.9	75
»	20 800	$Cu(acac)_3$	1.9	75
»	20 800	$Cu(dpm)_3$	0.5	75
Benzil	18 800	$Fe(acac)_3$	2.7	75
»	18 800	$Cr(acac)_3$	1.1	75
Fluorenone	18 650	$Cr(acac)_3$	1.2	75
Diacetyl	19 000	$Fe(acac)_3$	3.1	78
Benzophenone	24 200	$Pd(SB)_2$(planar)	3.0	72
Chrysene	20 000	ditto	2.3	72
1,2,3,4-Dibenzanthracene	17 800	»	1.4	72
Pyrene	16 900	»	<0.05	72
Acridine	15 800	»	<0.05	72
Anthracene	14 950	»	<0.05	72

Notation: dpm = dipivalomethanate; SB = Schiff bases with different substituents; tetr. = tetrahedral; oct. = octahedral; Hen-sam-OH = 

b. Effect of the Structure of the Organic Molecule and the Transition Metal Complex and of the Properties of the Solvent on the Rate of Energy Transfer

After the discovery of the method of flash photolysis of Norrish and Porter [71,72], numerous studies were published in which the rate constants for the quenching of triplet molecules by transition metal ions were determined by this procedure. As shown above, in most cases the quenching is due to energy transfer.

Table 6 presents the constants k_t for the transfer of triplet energy from aromatic hydrocarbons at room temperature. It shows that in most cases k_t is around 10^7-10^8 litre mole^{-1} s^{-1}, which exceeds by 1–3 orders of magnitude the analogous constant for the transfer of triplet energy from aromatic hydrocarbons to lanthanide ions [1,7,8,34,38]. The constant k_t increases by a further order of magnitude (to 10^9 litre mole^{-1} s^{-1}) in the quenching of triplet molecules by complexes of transition metal ions with aromatic ligands, as can be seen from the data in Table 7. The quenching is not associated with energy transfer to the triplet level of the ligand, because transfer processes of the latter type are strongly endothermic under the experimental conditions. Table 7 shows that the energy transfer to complexes with aromatic ligands is independent of the structure of the energy donor molecules, in particular of the presence in the latter of active carbonyl and other groups. This shows that the exchange-resonance interactions between the π system of the triplet molecule and the d shell of the transition metal ion takes place effectively via the π system of the coupled ligand. Steric hindrance to the mutual approach of the organic molecule and the π-electron system of the chelate, arising on passing from acetylacetonates to dipivalomethanates, leads to a decrease of k_t by a factor of 2–4 (Table 7).

Table 8. The rate constants for the quenching of triplet naphthalene molecules by transition metal ions in solvents of different viscosities at 293 K in the absence of molecular oxygen [38].

Quenching agent-acceptor	Solvent I and k_d	$10^{-7}k_t^I$, litre mole^{-1} s^{-1}	Solvent I and k_d	$10^{-7}k_t^{II}$, litre mole^{-1} s^{-1}
$[Ni(H_2O)_6]^{2+}$	Water ($k_d = 6.5\cdot10^9$ litre mole^{-1} s^{-1})	2.3	Ethylene glycol ($k_d = 3\cdot10^8$ litre mole^{-1} s^{-1})	2.3
$[Co(H_2O)_6]^{2+}$		5.0		4.4
$[Mn(H_2O)_6]^{2+}$		2.8		1.6
$[Cu(H_2O)_6]^{2+}$		7.5		7.3

The influence of the ligand on the quenching activity of copper(II) chloride has also been studied [77]. The authors observed that ethylenediamine used as a ligand decreases while o-phenanthroline increases the rate of quenching of the triplet state of anthracene.

The effect of complex formation on the quenching of triplet anthracene by Co^{2+}, Ni^{2+}, and Cu^{2+} ions in ethylene glycol at 298 K was studied by Yatsimirskii and Dagaev [79–81]. It was shown that the formation of complexes by the above ions with ethylenediamine, ethylenediaminetetra-acetate, diethylenetriaminepenta-acetate, and cyclohexanediaminetetra-acetate increases the quenching rate constant by a factor of 2–4.

It is at present impossible to reach definite conclusions about the effect of the structure of the complexes and the organic molecules on the rate of energy transfer, since none of the scientific schools have carried out systematic studies on this problem.

The problem of the effect of the solvent on the efficiency of energy transfer from triplet molecules to transition metal ions has also been little investigated. Nevertheless we believe that some data on this problem can be usefully mentioned. Since the rate constants k_t for energy transfer to transition metal complexes with non-aromatic ligands are lower by 1–3 orders of magnitude than the diffusion rate constants k_d, an increase in the viscosity of the solvent should not have an appreciable effect on k_t until k_d becomes smaller than k_t in solvents with a low viscosity. The data of Porter and Wright [38] quoted in Table 8 constitute an experimental confirmation of this conclusion. Evidently the change in viscosity by a factor of 20 on passing from water to ethylene glycol hardly affects k_t. One should bear in mind that an increase in the viscosity of the solvent usually leads to a simultaneous increase of the lifetime of the triplet molecules and is accompanied by an increase in the quantum yield of the energy transfer reaction‡ φ_t at the same energy acceptor concentration. Hence it is possible to increase φ_t by increasing the viscosity of the solvent—by changing it for a related solvent or by reducing the temperature. Admittedly the latter is possible only when the transfer process lacks an appreciable activation energy.

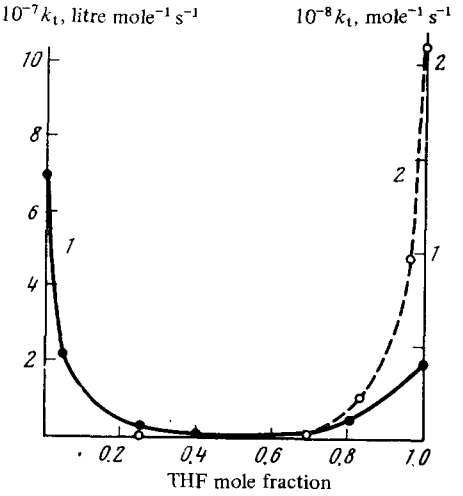


Figure 2. Dependence of the rate constant for the quenching of the triplet state (k_t) of naphthalene by cobalt(II) chloride (curve *1*) and of anthracene by cobalt(II) perchlorate (curve *2*) on the composition of the solvent (water–tetrahydrofuran) [34,73].

Although the rate of energy transfer from triplet molecules to transition metal ions was measured in different solvents (see Tables 3–8), it is at present difficult to

‡ We interpret the quantum yield of the energy reaction φ_t as the ratio of the number of transfer steps to the number of donor triplet molecules formed during the same period under quasisteady-state conditions.

reach any definite conclusions about the role of the chemical nature of the solvent in this process. However, one should note an early study by Linschitz and Pekkarinen [34] in which it was shown that k_t for energy transfer from anthracene and tetraphenylporphin triplets to transition metal ions in tetrahydrofuran and pyridine decreases by 1–3 orders of magnitude after the addition of water to the solvent (Fig. 2). On the other hand, Rogov et al. [73] recently investigated the influence of the addition of alcohols or ethers (Fig. 2) on the rate constant for energy transfer from naphthalene triplet to cobalt(II) complexes. Fig. 2 shows that k_t falls in this case too. There is at present no unambiguous explanation of this interesting phenomenon. Possibly effects associated with the ordering of the solvent molecules in the second coordination sphere of the transition metal ion play a significant role here.

IV. ENERGY TRANSFER BETWEEN TRANSITION METAL COMPLEXES AND MOLECULAR OXYGEN

Studies by Farmilo and Wilkinson [82] and Carlson et al. [83] have now firmly established that transition metal complexes are effective quenching agents for singlet molecular oxygen in solution. It has been shown that the quenching constants are independent of the method of preparation of singlet oxygen. The value of τ for singlet molecular oxygen was estimated by analysing the kinetics of the disappearance of the absorption of 1,3-diphenylazobenzofuran or rubrene in its presence.

Table 9. The constants for the quenching of singlet oxygen by transition metal ions in various solvents at 298 K according to the literature [82,83].

Quenching agent	Solvent	$10^{-8}k_t$, litre mole^{-1} s^{-1}
$Ni^{II}(SB)_2$	Benzene	30
$Pd^{II}(SB)_2$	Benzene	0.6
Di-(2-hydroxy-5-methoxyphenyl-N-n-butylaldimine)-nickel(II)	Iso-octane	35
	Hexadecane	2.0
Nickel(II) di-n-butyldithiocarbamate	Iso-octane	7.0
	Hexadecane	9.0
Nickel(II) n-butylamine[2,2′-thiodi-(4-t-octyl)-phenoxide]	Iso-octane	1.8–2.7
	Hexadecane	0.8
Nickel(II) acetylacetonate	Iso-octane	1.3–2.0
Nickel(II) di(*O*-butyl-3,5-di-t-butyl-4-hydroxybenzyl-phosphonate)	2-Butoxyethanol	0.34
$NiCl_2.6H_2O$	"	3.1
$CoCt_2.6H_2O$	"	0.48
$MnCl_2.4H_2O$	"	<0.01

Table 9 presents the constants for the quenching of singlet oxygen by complexes of different transition metals. The most effective quenching agents are nickel(II) complexes, whose resonance state lies below or possible in some cases at the same energy as O_2 ($^1\Delta g$). The efficiency of quenching by many nickel(II) complexes depends significantly on the ligand. The highest constants are observed for nickel(II) complexes with Schiff bases (SB). The complex $[Mn(H_2O)_6]^{2+}$, the excited resonance state of which is higher than the $^1\Delta g$ state of oxygen, does not quench singlet oxygen. Presumably the main process involved in the quenching of singlet oxygen by transition metal ions is, as for triplet organic molecules, radiationless transfer of electronic excitation energy, which proceeds via an exchange-resonance mechanism, bearing in mind that the $^1\Delta g \rightarrow {}^3\Sigma\bar{g}$ electronic transition in oxygen is forbidden.

Table 10. The rate constants for the quenching of the luminescence of chromium(III) complexes by oxygen extrapolated to 298 K (in the 2 : 1 : 1 mixture of methanol, water, and ethylene glycol as solvent) [84].

Energy donor	$10^{-9}k_t$, litre mole^{-1} s^{-1}	Energy donor	$10^{-9}k_t$, litre mole^{-1} s^{-1}
$[Cr(acac)_3]$	100**	$[Cr(CN)_6]^{3-}$	0.2
$[Cr(NCS)_6]^{3-}$	6	$[Cr(en)_3]^{3+}$	<0.01
{*trans*-$Cr(NH_3)_2(NSC)_4]^{1-}$	2	$[Cr(tmen)_3]^{3+}$ *	<0.01

*tmen = trimethylethylenediamine.

**The values of k_t for $Cr(acac)_3$ at 298 K is unreliable, since it was found by extrapolating to 298 K the values of k_t measured below 180 K.

The quenching of the phosphorescence of excited chromium(II) complexes by molecular oxygen was observed and studied by Pfeil [84]. He assumed that the quenching mechanism involves exchange-resonance energy transfer and explains the marked dependence of the rate constant for the quenching of the phosphorescence of the complexes by oxygen on the nature of the ligand in the complex (Table 10) by the different capacities of the ligands to conduct π electrons and hence by the different overlapping of the electron clouds of the energy donor and acceptor. However, comparison of the data in Table 10 with those in Table 6 makes it clear that σ-binding ligands such as NH_3 or ethylenediamine (en) do not prevent energy transfer from organic molecules to transition metal complexes. We believe that, in discussing the involvement of the ligand in energy transfer between complexes and O_2, one must take into account the possibility of the formation of unstable transition metal complexes with O_2 and the effect of this process on the energy transfer. Transition metals are known to exhibit a tendency to form complexes with O_2. [85]

V. APPLICATIONS OF RADIATIONLESS ENERGY TRANSFER IN THE STUDY OF PHOTOCHEMICAL REACTIONS OF COORDINATION COMPOUNDS OF TRANSITION METAL IONS

The photochemistry of the coordination compounds of transition metal ions has developed very vigorously in recent years. Starting with the pioneer study by Volger and Adamson [86] (1968), the method of radiationless energy transfer from organic molecules began to be used in the investigation of the mechanisms of photochemical reactions. The largest number of studies have been devoted to chromium(III) and cobalt(III) complexes, since the mechanisms of the direct photochemical reactions of such complexes have been investigated in greatest detail. Investigations dealing with certain other ions have also begun to appear in recent years. Brief reviews of the mechanisms of photosensitised reactions are contained in an excellent monograph on the photochemistry of coordination compounds by Balzani and Carassiti [87] and also in other surveys [88–91]. However, they are already obsolete owing to the vigorous development of this field.

1. THE ROLE OF ENERGY TRANSFER IN DETERMINING THE REACTIVITIES OF THE LOWEST EXCITED STATES OF TRANSITION METAL COMPLEXES

The spectroscopy of transition metal complexes has shown that, depending on the strength of the ligand field, the long-wavelength absorption band of the complexes may correspond both to a transition allowed by the spin selection rules and to a forbidden intercombination transition. In the latter case direct selective population of the lowest excited level of the complex by light is difficult, since it is impossible to separate the weak intercombination absorption from the stronger allowed absorption of the adjacent band. In many instances the application of radiationless energy transfer helps in overcoming these difficulties.

It can now be regarded as firmly established that organic molecules are capable of sensitising photochemical reactions of transition metal complexes by energy transfer both from excited singlet [43,44,46] and triplet [92] states.

The processes (for example photochemical aquation processes) occurring in a binary solution {organic sensitiser—energy donor (D) and the transition metal complex $[M^{k+}L_l]$} can be represented schematically as follows (it is assumed that under the experimental conditions the intrinsic absorption of the complex can be neglected compared with the absorption of the sensitiser):

Scheme I

$$^1D + h\nu \rightarrow {}^1D^*, \quad (I\text{-}1)$$

$$^1D^* + {}^n[M^{k+}L_l] \rightarrow {}^1D + {}^n[M^{k+}L_l]^*, \quad k_{ts}\ (I\text{-}2)$$

$${}^n[M^{k+}L_l]^* + H_2O \rightarrow [M^{k+}L_{l-1}H_2O] + L, \quad k_R(I\text{-}3)$$

$$^1D^* \rightarrow {}^1D + h\nu_{fl}, \quad k_{em}(I\text{-}4)$$

$$^1D^* \rightsquigarrow {}^3D, \quad k_{i.c.}(I\text{-}5)$$

$$^3D + {}^n[M^{k+}L_l] \rightarrow {}^1D + {}^m[M^{k+}L_l]^*, \quad k^I_{tT}(I\text{-}6)$$

$${}^m[M^{k+}L_l]^* + H_2O \rightarrow [M^{k+}L_{l-1}H_2O] + L, \quad k^I_R(I\text{-}7)$$

$$^3D + {}^n[M^{k+}L_l] \rightarrow {}^1D + {}^n[M^{k+}L_l]^*, \quad k^{II}_{tT}(I\text{-}8)$$

$${}^n[M^{k+}L_l]^* + H_2O \rightarrow {}^n[M^{k+}L_{l-1}H_2O] + L, \quad k^{II}_R(I\text{-}9)$$

$$^3D \rightsquigarrow {}^1D, \quad k_D\ (I\text{-}10)$$

where ^1D and ^3D are the singlet and triplet states of the sensitiser, M^{k+} is the transition metal ion, L is the ligand, n and m are the multiplicities of the states of the complex, and an asterisk designates electronically excited states.

Whether the photochemical reaction occurs via the singlet or triplet sensitisation channel depends on the ratios of the probabilities of all the processes involving the given excited state of the donor.

It is known from the energy transfer theory that, for effective energy transfer from the donor to the acceptor, two requirements must be met: an energy requirement—the level of the energy donor must lie above the level of the acceptor (the overlapping of the emission spectrum of the donor and the absorption spectrum of the acceptor must be a maximum)—and a spin requirement. For maximum efficiency of the inductive-resonance energy transfer from the excited singlet level of the donor, it is necessary that the multiplicities of the excited and ground states should be identical both in the donor molecule and in the acceptor complex; for exchange-resonance energy transfer, it is necessary that Wigner's rule (the overall spin of the system must remain unchanged) should hold for the transfer process.

The sensitisation of photochemical reactions of transition metal complexes by energy transfer from the excited singlet state of the organic molecule [40] is not of much interest for the elucidation of the mechanisms of such reactions, since it is equivalent (see Scheme I) to direct excitation of the complex in the region of its allowed absorption band.

The study of the dependence of the reactions of the complexes on the height of the triplet level of the sensitiser makes it possible in many instances to reach an unambiguous conclusion about the inertness or reactivity of the lowest excited states of transition metal complexes, i.e. about the energies of the photochemical activated states of non-phosphorescent complexes§.

We shall consider separately two different cases of energy transfer to transition metal complexes.

1. Transfer to low-spin complexes with a set of singlet and triplet energy states. In particular, cobalt(III), rhodium(III), and platinum(II) [94] complexes have zero spin in the ground state. In this case, according to Wigner's rule, of the two processes 6 and 8 in Scheme I only process 6, i.e. triplet–triplet energy transfer to these complexes, is allowed. Consequently the very fact that a sensitised photochemical reaction occurs in this case is unambiguous evidence for the reactivity of the triplet state of the complex. The involvement of the triplet states of the complexes $[Co(CN)_6]^{3-}$, $[Co(CN)_5X]^{2-}$ (where X = Br, Cl, I, or pyridine) [95,96], $[Rh(NH_3)_5X]^{2+}$ (where X = Br, Cl, or I), [92] and $[PtCl]^{2-}$ [97] in their photochemical aquation reactions was demonstrated by this method. In all these studies diacetyl was used as the sensitiser. The quenching of its phosphorescence in the presence of the complexes and the constant intensity of its fluorescence lead to the unambiguous conclusion that the triplet state of diacetyl is responsible for the sensitisation.

2. The transfer of triplet excitation energy to all stable low- and high-spin transition metal complexes with any set of multiplet states other than that considered in paragraph 1 above. In this case both energy transfer processes (processes 6 and 8 in Scheme I) are possible, according to Wigner's rule, for exchange-resonance energy transfer.

If the energy gap between the two lowest excited levels of the transition metal ion is fairly large (>2400 cm^{-1}, see Moggi and Balzani [90]), the reactivity of the lowest excited state of the ion can be determined by studying the dependence of the sensitisation of the photochemical reaction on the height of the triplet level of the sensitiser. This method was used in the investigation of the relative reactivities of the doublet and quartet states of chromium(III) complexes. Diacetyl, acridine, Michler's ketone, and Methylene Blue were used as sensitisers for the complex $[Cr(NH_3)_5NCS]^{2+}$; [43] $[Cr(CN)_6]^{3-}$ was sensitised by pyrazine, xanthone, Michler's ketone, anthracene, and $[Ru(bipy)_3]^{2+}$. [59,98] Among these sensitisers, diacetyl, acridine, pyrazine, and xanthone, i.e. the compounds whose triplet level lies above the $^4T_{2g}$ level of Cr^{3+}¶ show the greatest ability to induce the photochemical aquation of the chromium(III) complexes. This result indicates the photochemical activity of the $^4T_{2g}$ level of Cr^{3+}. The demonstration of the low probability of the aquation reaction via the ^2E_g level follows from a comparison of the

§ Only a few transition metal complexes are phosphorescent in liquid solutions [93].

¶ The failure of Michler's ketone, whose triplet level is also above the $^4T_{2g}$ level, to cause sensitisation is probably due to the short lifetime of its triplet state in solution, i.e. $k_{tT}[M] < \tau_{^3I}^{-1}$.

data for the ability of anthracene and the complex $[Ru(bipy)_3]^{2+}$ to sensitise the phosphorescence of $[Cr(CN)_6]^{3-}$ in dimethylformamide at a reduced temperature with data concerning the absence of the photosensitised photochemical aquation reaction in the systems $[Ru(bipy)_3]^{2+}$ (sensitiser)$-[Cr(CN)_6]^{3-}$ in water and anthracene$-[Cr(CN)_6]^{3-}$ in dimethylformamide. All the considerations adduced here for the photochemical aquation reaction are equally valid for the photochemical isomerisation of transition metal complexes.

The situation is more complex in the sensitisation of the photochemical reduction reaction, for example the photochemical reduction of the amino-complexes of cobalt(III) which takes place on excitation of the triplet states of diacetyl, biphenyl, and quinoline[41,99]. Together with energy transfer and subsequent reduction of cobalt from the tervalent to the bivalent state in the complex itself (see process 1 in Scheme II), type 2 electron transfer is also possible in this system.

Scheme II

$$^3D + [Co(NH_3)_6]^{3+} \rightarrow {}^1D + {}^3([Co(NH_3)_6]^{3+})^* \xrightarrow{+\text{solv.}} {}^1D + [Co(NH_3)_6]^{2+}, \quad (II-1)$$

$$^3D + [Co(NH_3)_6]^{3+} \rightarrow {}^2D^+ + [Co(NH_3)_6]^{2+} \xrightarrow{+\text{solv.}} {}^1D + [Co(NH_3)_6]^{3+}. \quad (II-2)$$

Unambiguous information about the reactivities of the different levels of the cobalt(III) complex can be obtained after eliminating process (II–2). For each specific system, the problem of the relative rates of energy and electron transfer requires special consideration. The same difficulty arises in attempts to investigate the photochemical reduction of Fe^{3+} by the energy transfer method.

2. THE QUANTUM YIELDS OF SENSITISED PHOTOCHEMICAL REACTIONS

Additional information about the pathways followed in photochemical reactions and the probabilities of intercombination transitions in complexes is provided by a comparison of the quantum yields of photochemical reactions in direct photolysis (φ_{ph}^{dir}) and in the sensitisation of the lowest excited state of the complex (φ_{ph}^{sens}).

We shall consider the photochemical aquation reaction.

It is again necessary to deal separately with complexes which have a singlet ground state. For such complexes, the quantum yield of the photochemical aquation reaction in direct excitation $\varphi_{aq}^{dir} = q_{^3\Gamma}(K)\Phi_{aq}(^3\Gamma) + \Phi_{aq}(^1\Gamma^*)$, where $q_{^3\Gamma}(K)$ is the quantum yield in the formation of the triplet state of the complex, $\Phi_{aq}(^3\Gamma)$ the quantum yield in the aquation of the triplet state, and $\Phi_{aq}(^1\Gamma^*)$ the quantum yield in the aquation of the singlet excited state of the complex. Under the conditions of total transfer via triplet levels from the organic sensitiser to the complex, the quantum yield of the sensitised photochemical aquation reaction $\Phi_{aq}^{sens} = q_{^3\Gamma}(D)\Phi_{aq}(^3\Gamma)$, where $q_{^3\Gamma}(D)$ is the quantum yield for the formation of the sensitiser triplets.

In this case comparison of φ_{aq}^{dir} with $\varphi_{aq}^{sens} q_{^3\Gamma}^{-1}(D)$ permits definite conclusions concerning the mechanism of the photochemical process: (1) when $\varphi_{aq}^{dir} = \varphi_{aq}^{sens} q_{^3\Gamma}^{-1}(D)$, then presumably the triplet state of the complex is the only reactive state and $q_{^3\Gamma}(K) = 1$; the alternative hypothesis that $\Phi_{aq}(^1\Gamma^*) = \Phi_{aq}(^3\Gamma)$ is less probable; the yields of the direct and diacetyl-sensitised reactions were found to be the same for the rhodium(III), platinum(II), and cobalt(III) complexes of the type $[Rh(NH_3)_5X]^{2+}$ (X = Cl^-, Br^-, or I^-),[92] $[Co(CN)_5Y]^{2-}$ (Y^- = N_3^-, NCS^-, or CN^-),[95] and $[PtCl_4]^{2-}$;[97] (2) when $\varphi_{aq}^{dir} < \varphi_{aq}^{sens} q_{^3\Gamma}^{-1}(D)$, it follows that $q_{^3\Gamma}(K) \leq \varphi_{aq}^{dir}/\varphi_{aq}^{sens} q_{^3\Gamma}^{-1}(D)$. Assuming that the reaction proceeds only via the triplet state of the complex $[\Phi_{aq}(^1\Gamma^*) = 0]$, it is possible to obtain $q_{^3\Gamma}(K)$ by comparing the yields of the direct and sensitised reactions. Such estimates of $q_{^3\Gamma}(K)$ have been made for $[Co(CN)_6]^{3-}$ [95] and $[PtCl_4]^{2-}$.[97] However, the data of Scandola and Scandola[95] conflict with the results of measurements of Wrighton et al.[96] (Table 11). (3) When $\varphi_{aq}^{dir} > \varphi_{aq}^{sens}$, the implication is that the singlet excited state of the complex is actively involved in the photochemical aquation process and $\Phi_{aq}(^1\Gamma^*) > \Phi_{aq}(^3\Gamma)$.

Among the transition metal complexes which do not have a singlet ground state, chromium(III) compounds were investigated in greatest detail. It was already noted above

Table 11. Comparison of the quantum yields of the direct and sensitised (by energy transfer from the triplet state of organic molecules) photochemical aquation reactions of transition metal complexes.

Complex $[M^{III}X_nY_m]$	Medium	Region of direct excitation	φ_{aq}^{dir} for different substituents		Sensitiser	φ_{aq}^{sens} for different substituents		References
			X	Y		X	Y	
$[Cr(NH_3)_6]^{3+}$	H_2O + EtOH (1:1), 298 °K, 0.03*N* $HClO_4$	$^4T_{2g} \leftarrow {}^4A_{2g}$	0.24		Naphthalene	0.18		76
$[Cr(NH_3)_5Cl]^{2+}$	ditto	ditto	0.35		ditto	0.34		76
$[Cr(NH_3)_5NCS]^{2+}$	H_2O + 0.1 *N* H_2SO_4, Ar, 298 °K	»	0.21	$9.5\cdot10^{-4}$	Diacetyl	0.21	$<10^{-4}$	43
$[Cr(en)_3]^{3+}$	H_2O + (0.003 *N* $HClO_4$), 218 °K	»	0.4	—	ditto	0.8	—	60
$[Co(CN)_6]^{3-}$	H_2O, evacuated soln.	$^1T_{1g} \rightarrow {}^1A_{1g}$	0.31	—	»	0.23	—	96
$[Co(CN)_5]^{3-}$	ditto	ditto	0.31	—	»	0.80	—	95
$[Co(CN)_5N_3]^{3-}$	»	»		0.23	»	—	0.22	96
$[Co(CN)_5NCS]^{3-}$	»	»		0.2	»	—	0.18	96
$[Rh(NH_3)_5Cl]^{2+}$	H_2O (0.002*M* $HClO_4$), Ar, 298 °K	$^1T_1 \leftarrow {}^1A_1$	$<10^{-3}$	0.15	»	$<10^{-3}$	0.16	92
$[Rh(NH_3)_5Br]^{2+}$	»	$^1E, {}^1A_2 \leftarrow {}^1A_1$	0.18	0.019	»	0.20	0.02	92
$[Rh(NH_3)_5I]^{2+}$	»	$^1E \leftarrow {}^1A_1$	0.86	0.01	»	0.90	—	92
trans-$[Rh(NH_3)_4I_2]^{1+}$	»	$^1T_1 \leftarrow {}^1A_1$	—	0.48	»	—	0.59	92

X = NH_3, en, CN^-

that sensitisation via energy transfer from singlet levels with excitation of the quartet levels of chromium(III) is equivalent to direct excitation and measurement of the quantum yields of photochemical aquation in this case provides no new information about the relative reactivities of the ^2E_g and $^4T_{2g}$ levels of the complex. The observed difference between the yields of the direct and riboflavine-sensitised photochemical aquation of $[Cr(NH_3)_5Cl]^{2+}$ [44] conflicts with data of a study [101] where it was shown that the photochemical aquation quantum yield is independent of the exciting light wavelength and an investigation [43] where the values of φ_{aq}^{sens} and φ_{aq}^{dir} were found to be the same in sensitisation by the acridinium ion.

The quantum yields of the photochemical aquation of chromium(III) complexes with sensitisation via the triplet state of organic molecules were measured in a series of studies [43,60,76,102]. In this case

$$\varphi_{aq}^{sens} = \frac{k_{tT}^{II}}{k_{tT}^{I} + k_{tT}^{II}} \Phi_{aq}\ (^4T_{2g}) + \frac{k_{tT}^{I}}{k_{tT}^{I} + k_{tT}^{II}} \Phi_{aq}\ (^2E_g),$$

where k_{tT}^{I} and k_{tT}^{II} are rate constants for energy transfer from triplets with excitation of the doublets and quartets respectively (see Scheme I).

The presence of so many unknowns precludes a conclusion concerning the reactivities of the $^4T_{2g}$ and ^2E_g states on the basis of data for φ_{aq}^{sens} and φ_{aq}^{dir}. Possibly some information about the reactivities of mixed transition metal complexes can be provided by a study of the dependence of the composition of the products of the reaction of these complexes on λ_{exc}. Martin and Adamson [43] observed differences between the products of the photolysis of $[Cr(NH_3)_5NCS]^{2+}$ with excitation in the region of the $^4T_{2g}$ and ^2E_g bands.

Comparison of the photochemical reaction products of this salt for sensitisation with acridinium ions and diacetyl confirmed qualitatively the differences between the reactivities of the $^4T_{2g}$ and ^2E_g states observed in direct photolysis by light corresponding to the absorption bands for these states (Table 11). The authors conclude that the $^4T_{2g}$ and ^2E_g states are responsible for the photochemical aquation of the NH_3 and NCS^- groups respectively†.

A defect of this and many other studies quoted here is the lack of data for the intensity of the exciting light. On the other hand, the ratios of the rates of the photochemical reaction and the dark forward and reverse reaction depend on the intensity of the exciting light. Since the dark reaction of $[Cr(NH_3)_5(NCS)]^{2+}$ involves the displacement of NCS^- and the photochemical reaction involves predominantly the displacement of NH_3, the ratio of the reaction products should depend on I_{exc}.

3. THE QUENCHING OF THE PHOTOCHEMICAL REACTIONS OF TRANSITION METAL COMPLEXES BY ENERGY TRANSFER FROM THE LATTER

The method of suppressing a photochemical reaction by the introduction of a quenching agent supplements the sensitisation method. Its employment makes it possible to determine the position of the photochemically active state. The combination of the sensitisation and quenching methods yields information about the distortions of this state on excitation. For example, in the absence of sensitisation the *cis–trans* isomerisation of diglycinato-platinum(II) by organic molecules with a triplet state below 22 900 cm^{-1} and the absence of the quenching of the photochemical reaction of Pt^{2+} by Mn_{aq}^{2+} ions (18 900 cm^{-1}), while Ni_{aq}^{2+} ions do cause quenching (8900 cm^{-1})‡ provide information about the shift of the triplet state of platinum(II) on excitation [104].

The quenching method also makes it possible to estimate the contribution of the given state of the overall yields of the photochemical reaction of the complex. As for sensitisation, this method is particularly simple only for transition metal complexes with a set of singlet and triplet levels. In this case the method is analogous to the procedure involving the quenching of the triplet state of organic molecules [2-4].

For other sets of states, the method of quenching the photochemical reactions of transition metal ions by the molecular triplet states is again coupled with the difficulty of separating the processes involving energy transfer from the two lowest excited states of the transition metal ion. The closeness of τ_{fl} and τ_{phosph} for chromium(III) complexes at room temperature aggravates this difficulty still further. For the chromium(III) complexes which phosphoresce in liquid solutions, comparison of data for the influence of quenching agents on photochemical aquation and the phosphorescence of the complexes helps in obviating these difficulties. The employment of this method made it possible to study the pathways in the photochemical reaction of the Reinecke salt in various solvents at reduced temperatures {O_2 [101] and $[Cr(CN)_6]^{3-}$ [81] were used as quenching agents} and in the photochemical aquation of $[Cr(en)_3]^{3+}$ in water at 293 K [cobalt(II) and iron(II) salts served as the quenching agents [105]].

In order to determine the reactivities of the ^2E_g and $^4T_{2g}$ levels of chromium(III), data for the quenching of the phosphorescence of the Reinecke salt and $[Cr(en)_3]^{3+}$, the decrease of the duration of their phosphorescence, and the excitation of the sensitised phosphorescence of $[Cr(CN)_6]^{3-}$ were compared [101,105] with data for the suppression of their photochemical aquation in the presence of quenching agents. It was found that φ_{ph} changes in the presence of $[Cr(CN)_6]^{3-}$ or Ni^{2+} to a lesser extent than q_{phosph} and τ_{phosph} for the Reinecke salt and the complex $[Cr(en)_3]^{3+}$. The incomplete suppression of the photochemical aquation reaction on depopulation of the ^2E_g level of these salts by energy transfer to $[Cr(CN)_6]^{3-}$ is significant evidence in support of the photochemical activity of the $^4T_{2g}$ level of these chromium(III) complexes.

The high reactivity of the $^4T_{2g}$ level of hexacyanochromium(III) was demonstrated by Wasgestian [59], who investigated the effect of O_2 on τ_{phosph} and φ_{aq}^{dir} for the complex $[Cr(CN)_6]^{3-}$ in dimethylformamide at room temperature a and observed that τ_{phosph} for the solution decreases by a factor of 10 after evacuation, but the latter has no influence on φ_{aq}^{dir} for this complex. This result enabled him to claim that the ^2E_g state of $[Cr(CN)_6]^{3-}$ is not reactive. It is still not known whether this claim is true for all chromium(III) complex and whether the hypothesis of Porter et

† No difference in φ_{aq}^{dir} on excitation to the ^2E_g and $^4T_{2g}$ states were noted for the complexes $[Cr(en)_3]^{3+}$, $[Cr(NH_3)_6]^{3+}$, and $[Cr(urea)_6]^{3+}$. [86]

‡ The oxidation-reduction properties of these ions are similar.

al.[101] and Wasgestian[105] that the photochemical activity in the direct population of the ^2Eg level is due to a thermal intersystem crossing to the $^4T_{2g}$ level is correct. If the above conclusion is valid, then the total absence of the photochemical aquation of $[Cr(NH_3)_5(NCS)]^{2+}$ on excitation by sensitiser whose triplet levels lie below the $^4T_{2g}$ level but above the ^2E_g, which was discussed above, can probably be accounted for by the low probability of energy transfer from the sensitisers to the chromium(III) ions and not solely by the height of their levels.

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The data described above make it certain that the main cause of the quenching of the fluorescence of organic molecules in solutions by transition metal ions is the inductive-resonance mechanism of energy transfer. The important role of exchange-resonance energy transfer in the sensitisation of the phosphorescence of transition metal ions and of their photochemical reactions has also been convincingly demonstrated. It has been established that the rate constants for the exchange-resonance energy transfer from organic molecules to transition metal ions are lower than those for the energy transfer between organic molecules[2,4] but higher than the rate constants for energy transfer to lanthanide ions[1]. This result is consistent with the decrease of the overlapping of the π-electron clouds of organic molecules in the following sequence: (1) π electrons of another organic molecule > (2) d orbitals of transition metal ions > (3) strongly shielded f orbitals of lanthanide ions.

The application of the exchange-resonance energy transfer in the study of photochemical reactions made it possible to solve unambiguously the problem of the reactivities of individual energy levels of the ions for a number of rhodium(III), cobalt(III), platinum(III), and chromium-(III) complexes§. On the other hand, many problems still await solution: (1) only the first attempts have been made to elucidate the mechanism of the influence of the ligand on the exchange-resonance energy transfer; (2) the role of the solvent in such energy transfer is not clear; (3) the problem of whether several photochemical reactions can occur simultaneously via the same electronic state of the ion remains open; (4) it is not known whether a photochemical reaction involving an excited state of the complex proceeds as the result of the labilisation of the bonds in the latter or whether it proceeds via high vibrational levels of the ground state reached by internal conversion from the quartet state. The latter possibility is inconsistent with the experimental observation that deuteriation of amino-groups has no influence on the φ_{ph} for the complexes[92].

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§ The review does not deal with studies on energy transfer involving transition metal complexes whose lowest excited states are singlet and triplet charge transfer states[106–110]. We believe that energy transfer between such complexes and transition metal ions is analogous to the energy transfer between organic molecules and transition metal ions.

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The Cleavage of the Carbon-Oxygen Bond by Organomagnesium Compounds

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Studies on reactions involving the cleavage of the C-O bond by organomagnesium compounds (OMC) (Grignard and Norman reagents and Iotsich complexes), including the behaviour of ethers, open-chain acetals, and cyclic acetals in relation to the OMC, are reviewed. The mechanism of the cleavage of the ether linkage by OMC is discussed, attention being concentrated on the reaction of 1,3-dioxacyclanes with OMC, the complex-formation processes in the reaction of 1,3-dioxolans with Grignard reagents and Iotsich complexes, and also the mode of the cleavage of asymmetrically substituted 1,3-dioxacyclanes by these reagents.
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I. INTRODUCTION

Since the publication of the last review[1] on the cleavage of the C-O bond by organomagnesium compounds (OMC) the number of studies in this field has doubled and continues to grow. This is particularly due to the discovery of new preparative syntheses and also the fact that they yield additional information about the structure of OMC and the role of electrophilic catalysis and complex formation in reactions of OMC.

The available information about the chemistry of the O-C bond has been appreciably amplified by studies on the cleavage of cyclic acetals and some of their analogues by Grignard, Iotsich, and Norman reagents carried out in recent years in the USSR[2-27] and abroad[28-34]. Until recently it was not clear whether the Chichibabin-Elgazin-Spath reaction[35-43] can be applied in the series of 1,3-diheterocyclanes. The recommendation[44] that certain cyclic acetals be used as solvents for Grignard syntheses appeared to suggest a high stability of such acetals in relation to OMC. Nevertheless the wide distribution of cyclic acetal systems in nature, the systematic use of acetal protecting groups in carbohydrate and steroid chemistry, and the high and many-sided physiological activities of certain 1,3-dioxacyclanes impart urgency to the solution of these problems: the reactions of the cyclic acetal group leads to new ways of synthesising and modifying important groups of organic compounds. After the development of an industrial method for the synthesis of 2-methyl-1,3-dioxolan[45], the possibility of its employment as a useful chemical starting material became apparent. Against the background of continually expanding research on the polymerisation of trioxan and cyclic acetals and ethers, analysis of the conditions and characteristics of the cleavage of the C-O bond has acquired special importance. Such cleavage is the initial stage in any method of polymerising oxygen-containing heterocycles.

Studies published from 1960 to 1962 and partly in 1973 are discussed critically in the present review. Of the earlier publications, only those which had not been considered in previous reviews[1,46,47] are quoted.

Attention has been concentrated on the reactions of OMC with cyclic acetals, which reflect the trend which is at present dominant in this field. The review does not deal with the behaviour of OMC in relation to 1,4-dioxans, 1,3,5-trioxans, and derivatives of morpholines and orthoesters, since no new data appear to have been published on this subject in the above period. It also seemed undesirable to include in the review the reactions of esters and lactones, since the cleavage of their C-O bonds on interaction with OMC appears to be a secondary process for such compounds, which is not part of the reactions under consideration.

II. ETHERS

1. Reaction Mechanism

In principle, the R'-O-R'' molecule can be cleaved when either of two C-O bonds is acted upon by OMC. If, developing further the ideas described by Houben-Weyl[47], the reaction is regarded as the usual bimolecular nucleophilic substitution (S_N2) at the carbon atom of the group R':

$$R'-OR'' + \overset{-\delta}{R'''}-\overset{+\delta}{M}gX \rightarrow R'-R''' + R''-OMgX, \quad (1)$$

then one must naturally expect that this entails the rupture of the C-O bond where the carbon atom has a lower electron density or there is a greater scope for the distribution of the charge of the attacking anion. Unfortunately, the mode and mechanisms of the cleavage reactions of ethers have not been analysed so far in the literature, although the relevant facts are available (see previous reviews[1,46,47]). If account is taken of all the examples at present available, the conclusion reached is fairly unexpected: the cleavage of asymmetric ethers by OMC involves preferentially the C-O bond in which the carbon atom has the maximum electron density. In other words, the cleavage involves the formation of the most favourable carbonium ion. This is illustrated by examples (2)-(8):[1,48-53]

$$CH_3OC_6H_5 + CH_3MgI \rightarrow C_2H_6 + C_6H_5OMgI, \quad (2)$$

$$C_2H_5OC_6H_5 + C_6H_{11}MgBr \rightarrow C_2H_4 + C_6H_{12} + C_6H_5OMgBr, \quad (3)$$

$$n\text{-}C_8H_{17}OCH_2CH{=}CH_2 + C_6H_5MgBr \rightarrow C_6H_5CH_2CH{=}CH_2 + n\text{-}C_8H_{17}OMgBr, \quad (4)$$

$$C_6H_5OCH_2C_6H_5 + C_4H_9MgBr \rightarrow C_6H_5CH_2C_4H_9 + C_2H_5OMgBr, \quad (5)$$

$$CH_2{=}CHCH_2OC_6H_5 + C_6H_5MgBr \rightarrow CH_2{=}CHCH_2C_6H_5 + C_6H_5OMgBr\ , \quad (6)$$

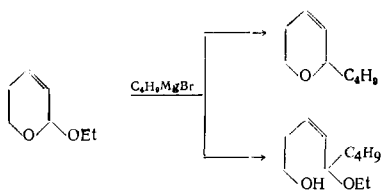
$$C_4H_9OCH_2CH{=}CHC_6H_5 + C_7H_{15}MgBr \rightarrow C_6H_5CH{=}CHCH_2C_7H_{15} + C_4H_9OMgBr\ , \quad (7)$$

$$(C_6H_5)_2COCH_2C \equiv CH + (C_6H_5)_2COCH_2C \equiv CMgBr \rightarrow$$
$$\rightarrow (C_6H_5)_2CC \equiv CCH_2OC(C_6H_5)_2 + HC \equiv CCH_2OMgBr\ . \quad (8)$$

Certain $\alpha\beta$-unsaturated ethers[54-56], which are sometimes cleaved on the side of the double bond, apparently constitute an exception. However, the contradictory information on this problem and also the known specificity of the chemical behaviour of such ethers preclude fairly definite conclusions. Thus it has been reported[55] that the ether $C_6H_5C(OC_2H_5){=}CH_2$ reacts with phenyl- and *p*-methoxyphenylmagnesium bromides, forming respectively $(C_6H_5)_2C{=}CH_2$ and $p\text{-}CH_3OC_6H_4(C_6H_5)C{=}CH_2$. It has also been shown[56] that alkyl vinyl ethers with different alkyl substituents in the α- and β-positions in the vinyl group are cleaved by Grignard reagents (GR) via the reaction

$$RCH{=}C(R')OR'' + R'''MgBr \rightarrow [RCH{=}C(R')OH] \rightarrow RCH_2COR'\ , \quad (9)$$

where R = H, $n\text{-}C_3H_7$, $n\text{-}C_5H_{11}$, or $n\text{-}C_6H_{13}$, R′ = H, $n\text{-}C_4H_9$, $n\text{-}C_5H_{11}$, or $n\text{-}C_6H_{13}$, R″ = C_2H_5 or $n\text{-}C_4H_9$, and R‴ = C_4H_9. Ultimately ketones formed. The reactants are heated in petroleum ether for 12–30 h.[56] For example, 5-undecanone was obtained in 76% yield from $C_5H_{11}CH{=}C(C_4H_9)OC_4H_9$ and butylmagnesium bromide. The results of the study by Quelet and d'Angelo[57] [reaction (10)] are consistent with this finding:



(10)

On the other hand, according to other data[58] β-alkyl-substituted vinyl ethers react with OMC to form primary alcohols and olefins. Similarly the reaction of unsubstituted vinyl ethers, in particular butyl vinyl ether, with phenylmagnesium bromide results in the formation of butanol and styrene in 60 and 30% yields respectively[56]. It has been suggested[56] that the yield of propenylmagnesium bromide, obtained in vinyl ethers, is influenced by its reaction with the solvent.

There are data on the polymerisation of vinyl ethers under the influence of Grignard reagents[59,60] showing that the polymerisation proceeds in the presence of an alkyl vinyl ether[60]. On the other hand, in the presence of an excess of the Grignard reagent, the initial ether is recovered unchanged even after heating and only a small amount of oligomers and products of the hydration of the vinyl ethers are formed under these conditions. Therefore, despite earlier studies[56,58], it was concluded[60] that alkoxy-groups adjoining the double bond are relatively immobile, like a halogen atom, and are not exchanged for the group in the OMC. These results for $\alpha\beta$-unsaturated ethers are nevertheless consistent with the conclusion that the majority of ethers react with OMC apparently via an S_N1 mechanism. However, since spontaneous dissociation of the C–O bond is unlikely under these conditions, the classical S_N1 mechanism must of course be rejected. The following explanation is probable. In all the known cases of the cleavage of the C–O bonds under the influence of OMC the reaction mixture contains Lewis acids (MgX_2 and CoX_2; here and henceforth X is a halogen), which are coordinated to the oxygen atom and probably ultimately cleave the C–O bond. This can occur simultaneously with attack by an anion†, for example R_2Mg:

$$Mg(R)_2 \longrightarrow R\overset{\curvearrowright}{O}{:}\,MgX_2\ . \quad (11)$$

In order to explain the observed mode of cleavage of asymmetric ethers, a decisive role must be attributed to the electrophilic attack $X_2Mg{\rightarrow}{:}O\langle$ in the dissociation of the C–O bond. Thus the process must be classified as nucleophilic substitution with electrophilic catalysis. As will be shown below, the majority of the characteristics of the dissociation of the C–O bond by OMC known at the present time can be explained satisfactorily by the proposed mechanism.

2. Cyclic Ethers

Like open-chain ethers, cyclic ethers are relatively unreactive in relation to OMC. It is not fortuitous that tetrahydrofuran (THF), 2-methyltetrahydrofuran, and tetrahydropyran occupy a special position as solvents for Grignard syntheses[44]. The following new facts can be added to the information available from previous reviews[1,46,47] on the behaviour of cyclic ethers in the presence of OMC. Many reactions involving OMC take place in THF without the cleavage of its ring[28,61,62]. Nevertheless it has been stated[63] that THF is cleaved when butylmagnesium bromide is synthesised in it. On the other hand, according to other data[44,64-67] THF begins to react with Grignard reagents only at about 200°C, forming primary alcohols:

$$+ RMgX \rightarrow R(CH_2)_4OMgX\ , \quad (12)$$

where

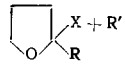
$$R{=}C_2H_5\,(Br),\ C_4H_9\,(Cl),\ (C_6H_5)_3C\,(Br);\quad X{=}Cl,\ Br\ .$$

Chlorotrimethylsilane and magnesium react in THF[68] via the mechanism

$$(CH_3)_3SiCl + Mg + \rightarrow (CH_3)_3Si(CH_2)_4OMgCl\ . \quad (13)$$

The reaction between dihydropyran and OMC leads to the formation of an unsaturated alcohol in 35–40% yield[69].

The reaction of 2-halogeno-substituted cyclic ethers with a Normal reagent can proceed in different ways. Thus, when $CH_3CH{=}CHMgBr$ interacts with 2-chlorotetrahydrofuran and 2-chlorotetrahydropyran, the unsaturated alcohols $CH_3CH{=}CHCH{=}CH(CH_2)_2OH$ and $CH_3CH{=}CHCH{=}CH(CH_2)_3OH$ are formed respectively[70]. On the other hand, another mode of this reaction has been described[71]:



$$+ R'MgBr \rightarrow + MgXBr\ , \quad (14)$$

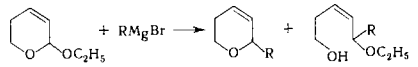
where R = H or CH_3, R′ = $CH_2{=}CH$ or $CH_3CH{=}CH$, and X = Cl or Br. The yield of the reaction products is 50%.

The reaction of 2-alkoxytetrahydropyrans with OMC has been studied[68,72] and the cleavage of the C–O bond in the pyran ring has been reported[69,73-76]. For example,

† One cannot rule out the possibility that this attack occurs in certain cases as a one-electron transfer.

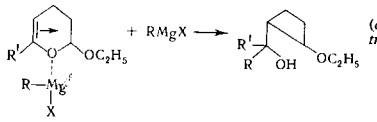
when 2-ethoxy-2,3-dihydro-γ-pyran is heated in toluene (85–90°C, 90 min) with an excess of a Grignard reagent, a mixture of *cis*- and *trans*-alkyl (or aryl)(2-ethoxycyclobutyl)methanols is formed in yields up to 48%.[74] The authors[74] suggest that the reaction proceeds via a mechanism involving cyclic electron transfer.

The reactions of the following cyclic ethers [reactions (15)–(20)] have also been described[28,57,77]:



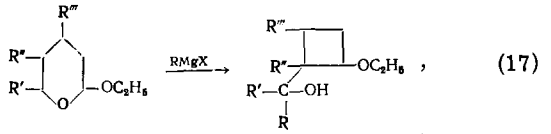
(15)

where R = CH_3, C_2H_5, n-C_4H_9, or C_6H_5;



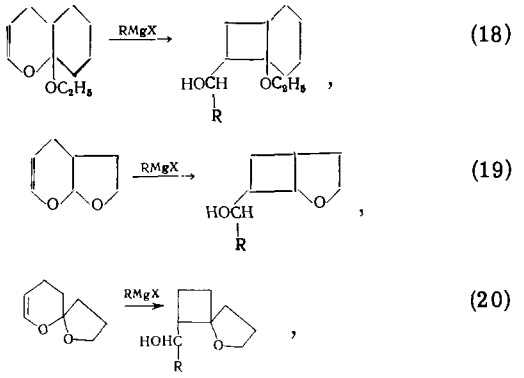
(16)

where R = CH_3, n-$C_4H_9C{\equiv}C$, or t-C_4H_9, R′ = H or CH_3, and X = Br or I;



(17)

where R = CH_3, C_2H_5, or C_4H_9, R′ = R″ = H, R‴ = CH_3 or C_6H_5, and X = Br or I;



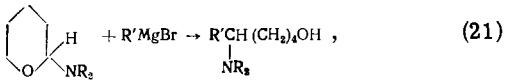
(18)

(19)

(20)

where R = C_2H_5 or C_4H_9 and X = Br.

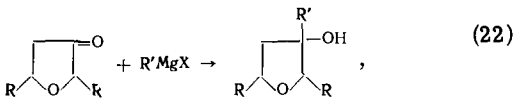
The interaction of 2-dialkylaminotetrahydropyrans with a Norman reagent leads to aminoalcohols[65]:



(21)

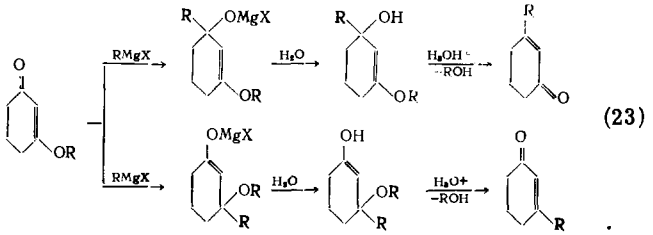
where R = C_2H_5 and R′ = $CH_2{=}CH$ or $CH_3CH{=}CH$.

Cyclic ketoethers react with OMC via the carbonyl group[78–80] [reactions (22) and (23)]:



(22)

where R = H or CH_3, R′ = CH_3, C_2H_5, C_3H_7, C_5H_{11}, or C_6H_5, and X = Br or Cl, and



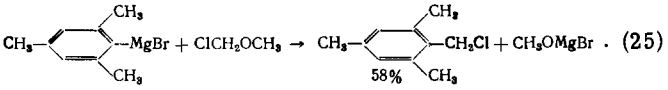
(23)

3. Ethers with Other Functional Groups

Full glycol ethers are fairly resistant to the action of OMC[81–83]. Thus the diethyl and dibutyl ethers of ethylene glycol[82], the diethyl and dibutyl ethers of diethylene glycol[66], and also the ethers of polyethylene glycols of the type $R(OCH_2CH_2)_nOR$ have been suggested[64] as high-boiling solvents for Grignard syntheses. The cleavage of the C–O bond under the influence of OMC was not observed in the dimethyl ether of ethylene glycol[81] even on heating at 70°C for 3.5 h. However, this ether is known to be cleaved appreciably[84] after 3 h at 95°C:

$$CH_3OCH_2CH_2OCH_3 + C_4H_9C{\equiv}CMgBr \rightarrow CH_3OCH_2CH_2C{\equiv}CC_4H_9 + CH_3OMgBr\,. \quad (24)$$

Halogenoethers. Without repeating the references quoted in Pokonova's monograph[85] and Summers' review[86], we shall examine the characteristic reactions of OMC with halogenoethers using some new examples. α-Chloroethers are known[85] to exchange their halogen readily for the hydrocarbon group in OMC, as a rule without the cleavage of the C–O bond. According to Shostakovskii et al.,[87] aryl α-chloroisopropyl ethers behave in this way. The reaction with Norman[88] and Iotsich[89–92] reagents proceeds similarly. Both halogen atoms are substituted without much difficulty in bis-(α-halogenomethyl) ethers[83]. However, under the influence of di-o-substituted arylmagnesium halides, the α-halogenoether is cleaved at the C–O bond[93,94]:



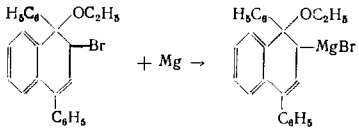
(25)

o-Halogenoethers form Grignard reagents[95]. When an attempt is made to prepare OMC from β-halogenoethers, the C–O bond is usually cleaved with the liberation of an olefin[96]:

$$CH_3O(CH_2)_4Cl + Mg \xrightarrow[THF]{ether} CH_3OMgCl + \rangle C{=}C\langle\,. \quad (26)$$

However, according to Shostakovskii et al.,[61] β-bromoethyl phenyl ether can react normally with magnesium.

Another instance of the formation of OMC from a β-halogenoether is also known[97]:



(27)

A Grignard reagent could not be obtained from γ-bromobutyl vinyl ether (in diethyl ether and THF as solvents), dimerisation and dehydrobromination products being detected[23,98]:

$$CH_2{=}CHO(CH_2)_3CHBrCH_3 + Mg \rightarrow CH_3{=}CHO(CH_2)_2CH{=}CHCH_3 + CH_2{=}CHO(CH_2)_3(CH_3)CHCH(CH_3)(CH_2)_3OCH{=}CH_2\,. \quad (28)$$

Only δ-bromobutyl vinyl ether reacts with magnesium without appreciable complications, forming the corresponding Grignard reagent[23,98].

A Norman reagent does not disrupt the C–O bond in $\alpha\beta$-dibromoethers[99,100] and certain Iotsich complexes behave similarly with respect to β-bromoethyl chloromethyl ether[101].

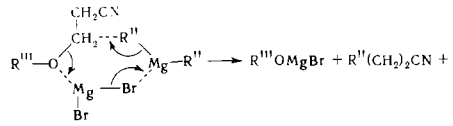
Certain trihalogenoalkyl ethers merely exchange their α-halogen atom for the alkyl group on reaction with a Grignard reagent and the C–O bond remains unaffected[28,102].

Ethers with active functional groups react with OMC in accordance with the general rule, i.e. via the most reactive fragment[28,103-106].

Cyanoethers. In contrast to α-alkoxynitriles, which react with OMC in the usual way, β-alkoxynitriles are wholly cleaved by the latter at the C–O bond[107]:

$$CH_2{=}CHOR'O(CH_2)_2C{\equiv}N + R''MgBr \rightarrow CH_2{=}CHOR'OMgBr\ , \qquad (29)$$

where R′ = $(CH_2)_2$ or $(CH_2)_2O(CH_2)_2$ and R″ = C_2H_5, C_4H_9, or C_6H_5. The reaction proceeds with evolution of heat. It has been suggested[107,108] that it involves the intermediate complex illustrated below:



$$\rightarrow R'''OMgBr + R''(CH_2)_2CN + R''MgBr\ , \qquad (30)$$

where R‴ = CH_2 or CHOR′.

The cyano-product obtained on cleavage of the ether is then converted into a ketiminate and which then polymerises:

$$R''(CH_2)_2CN \rightarrow \left[\begin{array}{c} -C(R')-NH- \\ | \\ (CH_2)_2R'' \end{array}\right]_n^- \ . \qquad (31)$$

When the β-cyanoethyl ether of 2-methyl-4-trimethylsilylbut-3-yn-2-ol reacts with ethylmagnesium bromide[109,110], the main process is the cleavage of the C–O bond:

$$(CH_3)_3SiC{\equiv}CC(CH_3)_2OCH_2CH_2CN + C_2H_5MgBr \rightarrow$$
$$\rightarrow (CH_3)_3SiC{\equiv}CC(CH_3)_2OH + (CH_3)_3SiC{\equiv}C(CH_3)_2OCH_2CH_2\underset{22\%}{\underset{\|}{C}}C_2H_5 \qquad (32)$$
$$O$$

Aminoethers. The exchange of the alkoxy-groups in certain aminoethers for the substituent in Grignard and Norman reagents has been described[111-115] [reactions (33)–(36)]:

$$H_2NOCH_3 + RMgX \rightarrow RNH_2 + CH_3OMgX\ , \qquad (33)$$

where R = C_2H_5, i-C_5H_{11}, i-C_4H_9, or t-C_4H_9 and X = Cl, Br, or I;

$$C_6H_5CH_2ONH_2 + RMgX \rightarrow RNH_2 + C_6H_5CH_2OMgX\ , \qquad (34)$$

where R = C_2H_5, i-C_5H_{11}, cyclo-C_6H_{11}, C_6H_5, $C_6H_5CH_2$, p-BvC_6H_4 or α-naphthyl and X = Cl, Br, or I;

$$R_2NCH_2OR + R''MgCl \rightarrow R_2NCH_2R'' + ROMgCl\ , \qquad (35)$$

$$R_2NCH(R')OR'' + R'''MgBr \rightarrow R_2NCH(R')R''' + R''OMgBr\ , \qquad (36)$$

where R = CH_3, C_2H_5, C_4H_9, C_5H_{11}, R′ = H, R″ = C_2H_5, C_4H_9, or C_6H_5, R‴ = $CH_3CH{=}CH$, $CH_2{=}CHCH_2$; $CH_2{=}CH$, $(CH_3)_2CH$, $(CH_3)_2C{=}CH$, i-C_5H_{11}, C_4H_9, or α-naphthyl, and X = Cl, Br, or I.

III. OPEN-CHAIN ACETALS AND THEIR STRUCTURAL ANALOGUES

Many acetals are very resistant to the reaction of OMC and it is difficult to make them undergo exchange reactions with the latter.

1. Formals

Dimethyl and diethyl formals nevertheless exchange alkoxy-groups for the substituent in the Grignard reagent at high temperatures, forming ethers[116-118]:

$$ROCH_2OR + C_6H_5MgBr \rightarrow C_6H_5CH_2OR + ROMgBr\ , \qquad (37)$$

where R = CH_3 or C_2H_5.

Saturated symmetrical formals derived from alcohols ranging from propanol upwards hardly react with OMC under these conditions. The method of synthesis of a number of OMC[119] in di-isopropyl or di-isobutyl formals is based on this finding. Mixed unsaturated formals[60] are more reactive than saturated symmetrical formals towards Grignard reagents. Alkoxy-groups containing multiple bonds then undergo exchange:

$$ROCH_2OR' + C_6H_5MgX \rightarrow R'OCH_2C_6H_5 + ROMgX\ , \qquad (38)$$

where R = C_2H_5 or C_4H_9 and R′ = $C(CH_3)_2CH{=}CH_2$, or $CH{\equiv}C(CH_3)_2C$.

The above data are consistent with the proposed mechanism (see Section I, 1), since of the two most probable intermediate cations of the type $ROCH_2^+$ the more stable is the one containing a group with more marked electron-donating properties (i.e. in the present case an aliphatic group). When an OMC acts on the diformals $ROCH_2OCH_2OR$, the corresponding formaldehyde acetals are formed in yields up to 50%:[120]

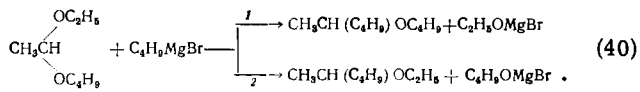
$$ROCH_2OCH_2OR + R'MgX \rightarrow ROCH_2OCH_2R' + ROMgX\ , \qquad (39)$$

where R = C_2H_5, C_4H_9, i-C_5H_{11}, or C_6H_{13}, R′ = $CH_2C_6H_5$ or n-C_6H_{13}, and X = Cl. This reaction proved to be convenient for the synthesis of formals with a β-phenylethyl alcohol residue, which has a flowery scent.

2. Acetaldehyde Acetals

In the reaction of symmetrical dialkyl and di(arylalkyl) acetals[121] with Grignard reagents the alkoxy-groups can be arranged in the following sequence in terms of the ease of their exchange: $OC_6H_5 > OAlk > OCH_2C_6H_5$. This sequence might have been foreseen on the basis of the ideas described in Section I.1. The available data on the reactivities of dialkyl acetals in relation to Grignard reagents are contradictory. Thus as early as 1961 Blomberg and Vrengdenhill[122] observed in the synthesis of Grignard reagents in boiling dialkyl acetals the cleavage of the latter with formation of ethers and alkoxymagnesium halides. However, in 1964 Shostakovskii et al.[123] suggested that diethyl and dibutyl acetals may be used as the medium for the synthesis of OMC, since according to their data, these acetals do not interact with Grignard reagents even at 150°C. Grinberg[124] obtained ethers derived from alkyl(aryl)hexylmethanols and diaryl(alkyl)hexylmethanes by the reaction between the acetal of oenanthaldehyde and OMC. Thus not only the acetal but also the ether formed from it are cleaved in this case.

If the alkyl groups in asymmetric acetals do not differ appreciably in their structures, the reaction proceeds in two ways[59]:



$$\rightarrow CH_3CH(C_4H_9)OC_4H_9 + C_2H_5OMgBr$$
$$\rightarrow CH_3CH(C_4H_9)OC_2H_5 + C_4H_9OMgBr\ . \qquad (40)$$

Pathway *1* is dominant, i.e. the less electron-donating alkoxy-group again undergoes exchange more readily. As expected, in mixed alkyl aryl acetals[59] the aryloxy-group

is split off preferentially. On the basis of the mechanism discussed in Section I.1, the symmetrisation of the mixed acetals in the course of these reactions might have been predicted. Such symmetrisation has in fact been observed in the reaction of ethylmagnesium bromide with butyl ethyl and benzyl ethyl acetals[59]. The reaction of acetals with a Iotsich complex leads to the formation of acetylenic ethers[84,125,126]:

$$CH_3CH(OR)_2 + HC\equiv CMgBr \xrightarrow[1-3\ h]{95^\circ} HC\equiv CCH(CH_3)OR + ROMgBr\,, \quad (41)$$

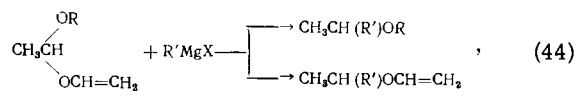
$$2CH_3CH(OC_4H_9)_2 + BrMgC\equiv CMgBr \rightarrow CH_3CH(OC_4H_9)C\equiv CCH(OC_4H_9)CH_3 + 2C_4H_9OMgBr\,. \quad (42)$$

The Iotsich complex obtained from ethynyldimethylmethanol is also reactive[127]:

$$CH_3CH(OC_4H_9)_2 + BrMgC\equiv CC(CH_3)_2OMgBr \xrightarrow{90-95^\circ} \rightarrow (CH_3)_2C(OH)C\equiv CCH(CH_3)OC_4H_9 + C_4H_9OMgBr\,. \quad (43)$$

The reactivity of C–O bonds in relation to the Iotsich complex increases sharply on passing from acetals to ketals[84]. It will be shown below that this rule holds fairly clearly also in other versions of the reaction of OMC with acetals or with their close analogues. This is yet another piece of evidence for the electrophilic nature of the rate-limiting stage in the cleavage of the C–O bond under the influence of OMC. Presumably, the interaction C–O←MgX_2, and not the nucleophilic attack $R^{\ominus}$→C–O, is decisive. Otherwise the enhancement of the electron-donating properties of the group joined to the oxygen atom on passing from acetals to ketals would have reduced the reactivity of the reacting C–O bonds. In reality the C–O bonds in ketals are more reactive than in acetals.

The acetals of unsaturated alcohols react with OMC like the acetals of saturated alcohols. The interaction of alkyl vinyl acetals with Grignard reagents[127,128] leads mainly to the formation of saturated ethers:



$$+ R'MgX \rightarrow \begin{cases} \rightarrow CH_3CH(R')OR \\ \rightarrow CH_3CH(R')OCH=CH_2 \end{cases}, \quad (44)$$

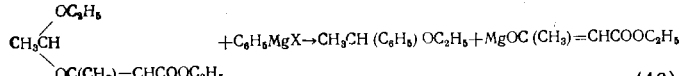
where R = alkyl or CH = CH, R′ = C_6H_5, and X = Br.

The yield of the corresponding alkyl vinyl ethers is about 30%, i.e. as in αβ-unsaturated formals[60], the C–O bond on the side of the more strongly electron-accepting group is the first to be broken, which is equivalent to the formation of the most stable carboxonium ion.

Divinyl acetals[127] involved in an exchange reaction with OMC form vinyl ethers:

$$CH_3CH(OCH=CH_2)_2 + RMgX \rightarrow CH_3CH(R)OCH=CH_2 + CH_2=CHOMgX\,. \quad (45)$$

It is surprising that the reaction of the acetal derived from the β-hydroxycrotonic ester with a phenylmagnesium halide[129] proceeds without affecting the ester group.



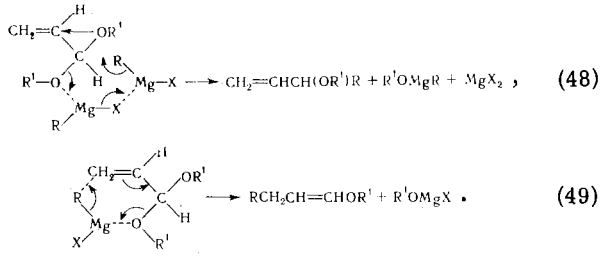
$$+ C_6H_5MgX \rightarrow CH_3CH(C_6H_5)OC_2H_5 + MgOC(CH_3)=CHCOOC_2H_5\,. \quad (46)$$

3. Acetals of Unsaturated Aldehydes

Acrolein acetals[130] give rise to a mixture of allyl and vinyl ethers on reaction with OMC:

$$CH_2=CHCH(OR')_2 + RMgX \rightarrow \begin{cases} \xrightarrow{1} CH_2=CHCH(R)OR' \\ \xrightarrow{2} RCH_2CH=CHOR' \end{cases}, \quad (47)$$

where R = CH_3, C_2H_5, C_3H_7, i-C_3H_7, C_4H_9, i-C_4H_9, $CH_3(C_2H_5)CH$, $(CH_3)_3C$, cyclo-C_6H_{11}, C_6H_5, $CH_3CH=CH$, or $C_4H_9C\equiv C$, R′ = CH_3, C_2H_5, i-C_3H_7, or $CH(CH_3)_2$, and X = Br, Cl or I. At elevated temperatures (100–120°C) pathway *1* predominates (the yield of allyl ether is 93%). The reaction is carried out in ether, THF, toluene, xylene, or decalin in the course of 1.5–2 h. The following reaction mechanisms have been proposed[130]:



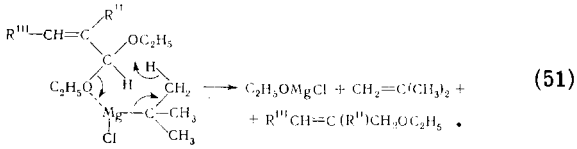
$$\rightarrow CH_2=CHCH(OR')R + R'OMgR + MgX_2\,, \quad (48)$$

$$\rightarrow RCH_2CH=CHOR' + R'OMgX\,. \quad (49)$$

The homologues of the propenal acetal[131] react with OMC as follows:

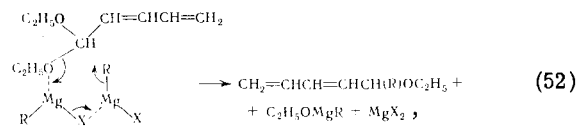
$$R^{IV}CH=CR^{III}CR^{II}(OR^{I})_2 + RMgX \rightarrow R^{IV}CH=CR^{III}CR^{II}(R)OR^{I} + RR^{IV}CHR^{III}C=C(R^{II})OR^{I}, \quad (50)$$

where R = C_2H_5, n-C_4H_9, $(CH_3)_3C$, C_6H_5, $C_6H_5CH_2$, or $C_6H_5CH_2CH_2$, R^I = C_2H_5, R^{II} = H or CH_3, R^{III} = H, C_2H_5, or i-C_3H_7, R^{IV} = H, and X = Br or Cl. The following reaction mechanism is discussed in the same study[131]:



$$\rightarrow C_2H_5OMgCl + CH_2=C(CH_3)_2 + R^{III}CH=C(R^{II})CH_2OC_2H_5\,. \quad (51)$$

Quelet and d'Angelo[57] proposed the mechanism



$$\rightarrow CH_2=CHCH=CHCH(R)OC_2H_5 + C_2H_5OMgR + MgX_2\,, \quad (52)$$

where R = CH_3, n-C_4H_9, or t-$C_4H_9C\equiv C$, and X = Br. Similar reactions are discussed in Normant's review[28].

Ethers with an acetylenic linkage have been obtained from propargyl acetals[132,133].

4. Halogenocetals

The acetals of halogenoaldehydes with a halogen atom in the β-position relative to the ethylidene group undergo an exchange reaction with OMC, forming β-halogenoethers[102]:

$$XCH_2CH(OR)_2 + R'MgX \rightarrow XCH_2CH(R')OR + ROMgX\,, \quad (53)$$

where R = n-C_4H_9, R′ = C_6H_5 or C_4H_9, and X = Br.

Under these conditions, the exchange takes place more readily than for the usual acetals. At first sight this finding is inconsistent with the fact that the C–O bond is ruptured before a new C–C bond is formed. However, when account is taken of the possibility of the anchimeric cooperation by the halogen atom,

$$XCH_2\overset{+}{C}H-OR \leftrightarrow CH_2-\underset{X^+}{CH}-OR\,, \quad (54)$$

the contradiction is removed.

In reactions with Iotsich complexes, bromoacetaldehyde acetals exchange their alkoxy-groups for the ethynyl group[125]. The bromine atom is not substituted under these conditions:

$$BrCH_2CH(OC_4H_9)_2 + HC\equiv CMgBr \rightarrow BrCH_2CH(C\equiv CH)OC_4H_9 + C_4H_9OMgBr, \quad (55)$$

$$2\,BrCH_2CH(OC_4H_9)_2 + BrMgC\equiv CMgBr \rightarrow 2C_4H_9OMgBr + \\ + BrCH_2CH(OC_4H_9)C\equiv CCH(OC_4H_9)CH_2Br. \quad (56)$$

The reactions of chlorodiphenylacetaldehyde with phenylmagnesium bromide, leading to acetals derived from carbon monoxide [$C(OR)_2$] and $\alpha\beta$-unsaturated ethers, have been described[134,135]:

$$(C_2H_5O)_2CHC(C_6H_5)_2Cl + C_6H_5MgBr \rightarrow (C_2H_5O)_2CHC(C_6H_5)_2MgBr + C_6H_5Cl \rightarrow \\ \rightarrow C(OC_2H_5)_2 + CH(C_6H_5)_2MgBr, \quad (57)$$

$$(C_6H_5O)_2CHC(C_6H_5)_2Cl + C_6H_5MgBr \rightarrow (C_6H_5O)_2CHC(C_6H_5)_2MgBr + C_6H_5Cl \rightarrow \\ \rightarrow C_6H_5OCH=C(C_6H_5)_2 + C_6H_5OMgBr. \quad (58)$$

However, studies by other workers[136] failed to confirm the existence of $C(OC_2H_5)_2$.

The interaction of the dibutyl acetal of bromoacetaldehyde with metallic magnesium leads mainly to butyl vinyl ether[60]:

$$BrCH_2CH(OC_4H_9)_2 + Mg \rightarrow CH_2=CHOC_4H_9 + C_4H_9OMgBr. \quad (59)$$

Similar reactions have been reported in other communications[137-139].

When α-bromoacrolein acetals are heated with Grignard reagents at 90–95°C for 3 h, unsaturated bromoethers are formed[131]:

$$CH_2=CHBrCH(OR')_2 + RMgX \rightarrow \begin{cases} \rightarrow RCHCBr=CHOR' \\ \rightarrow CH_2=CBrCH(R)OR' \end{cases}, \quad (60)$$

where R = C_4H_9, R′ = C_2H_5, and X = Br.

When a Grignard reagent reacts with the diethyl acetal of bromoacetaldehyde, β-bromovinyl ethyl ether is formed in 53% yield[28]:

$$Br_2CHCH(OC_2H_5)_2 \xrightarrow{i\text{-}C_5H_{11}MgCl} trans\text{-}CHBr=CHOC_2H_5. \quad (61)$$

The dimethyl acetal of α-bromo-β-chloropropionaldehyde exchanges only the methoxy-group in the cold for the group in the Grignard reagent[102]:

$$ClCH_2CHBrCH(OCH_3)_2 + RMgX \rightarrow ClCH_2CHBrCH(R)OCH_3 + CH_3OMgBr, \quad (62)$$

where R = n-C_3H_7 or n-C_4H_9.

The halogen in the acetals of chloropropiolaldehyde may be substituted by the group of the Grignard reagent with formation of acetals of $\alpha\beta$-acetylenic aldehydes in 40–70% yield[139]:

$$ClC\equiv CCH(OR)_2 + R'MgX \rightarrow R'C\equiv CCH(OR)_2 + MgXCl, \quad (63)$$

where R = C_2H_5 or C_4H_9, R′ = n-C_3H_7, i-C_3H_7, n-C_4H_9, i-C_4H_9, n-C_6H_{13}, n-C_9H_{19}, C_6H_5, or α-$C_{10}H_7$ and X = Br.

The acetals of halogenoalcohols as a rule exchange their halogen atom for the group of the OMC in the first place. Thus the reaction

$$CH_2CH(OR)OCH_2CH_2Cl + R'MgX \rightarrow \begin{cases} \rightarrow CH_2CH(R')OCH_2CH_2Cl \\ \rightarrow CH_2CH(OR)OCH_2CH_2R' \\ \rightarrow CH_2CH(R)OCH_2CH_2R', \end{cases} \quad (64)$$

where R = C_2H_5 or C_4H_9, R′ = C_6H_5 or $C_6H_5CH_2$, and X = Cl or Br, has been described[140]. The reaction temperature is higher than the boiling point of β-chloroethyl acetal.

When di-(β-chloroethyl) acetal reacts with benzylmagnesium chloride, both chlorine atoms are substituted by benzyl residues with formation of di-(γ-phenylpropyl) acetal[141-143]:

$$CH_3CH(OCH_2CH_2Cl)_2 + 2\,RMgX \rightarrow CH_3CH(OCH_2CH_2R)_2 + 2MgClX, \quad (65)$$

where R = C_6H_5 or $C_6H_5CH_2$ and X = Br or Cl.

Asymmetric alkyl β-chloroethyl acetals react similarly with Grignard reagents[141], but the yield of substitution products does not exceed 8%. The authors[141] note that chlorine in the β-position relative to the alkoxy-group makes the latter relatively immobile.

After prolonged heating with magnesium in ether, alkyl β-chloroethyl acetals give rise to a mixture of three products[60]:

$$2CH_3CH(OC_4H_9)OCH_2CH_2Cl + Mg \rightarrow \begin{cases} 1 \rightarrow CH_3CH(OC_4H_9)OCH_2CH_2CH(CH_3)OCH_2CH_2Cl \\ 2 \rightarrow CH_3CH(OC_4H_9)OCH_2CH_2CH_2CH_2OCH(OC_4H_9)CH_3 \\ 3 \rightarrow ClCH_2CH_2OCH(CH_3)CH(CH_3)OCH_2CH_2Cl. \end{cases} \quad (66)$$

The third pathway predominates.

5. Acetals with Other Functional Groups and Heteroatoms

The acetals of methoxyacetaldehyde[106] form glycol ethers with OMC:

$$CH_3OCH_2CH(OCH_3)_2 + RMgCl \rightarrow CH_3OCH_2CH(R)OCH_3. \quad (67)$$

The reaction of the ethoxyacetals $C_6H_5[CH(OC_2H_5)CH_2]_n.CH(OC_2H_5)_2$ with $ArCH_2MgCl$ has been discussed[144,145] as a possible pathway to the synthesis of arylated polyene hydrocarbons, which are used as organic phosphors.

Carbamoyl- and cyano-acetals react with OMC via their functional groups[106,129,146]:

$$R_2NCOCH(OC_2H_5)_2 + CH_3MgI \rightarrow R_2NC(OH)(CH_3)CH(OC_2H_5)_2 \rightarrow (C_2H_5O)_2CHCCH_3, \quad (68)$$

$$CNCH(OR)_2 + R'MgX \rightarrow R'COCH(OR)_2, \quad (69)$$

where R = C_2H_5 or C_6H_5 and R′ = C_2H_5, i-C_3H_7, n-C_5H_{11}, n-C_7H_{15}, C_6H_5, or cyclo-C_6H_{11}. The yield of ketoacetals in the latter reaction is 79–95%.

At 36°C 1-acetoxy-1-butoxyethane reacts with Grignard reagents primarily via the ester group[140,147], which is ultimately exchanged for the group attached to the Grignard reagent.

Mono- and di-thioacetals can be involved in exchange reactions with OMC[148,149] [reaction (70)]. Monothioacetals initially split off the alkoxy-group under the influence of the Grignard reagent:

$$CH_3CH(OR')(SR'') + RMgX \rightarrow CH_3CH(R)SR'' + R'OMgX, \quad (70)$$

where R = C_4H_9 or C_6H_5. The reaction of dithioacetals with Grignard reagents is much more difficult.

The reaction of organosilicon acetals with OMC has been described[110,140,150]. The alkoxy-group containing the silicon atom is exchanged regardless of whether it is linked to oxygen directly or is more remote. This mode of reaction is difficult to explain. The corresponding ethers are usually obtained in yields up to 70%.

The capacity of organosilicon groups in acetals for exchange decreases in the sequence[150] $OSi(CH_3)_3 > OSi(C_2H_5)_3 > OCH(CH=CH_2)CH_2Si(CH_3)_2C_2H_5$.

In organogermanium acetals the germanium-containing groups are also exchanged for the group of the Grignard reagent[60].

IV. CYCLIC ACETALS (1,3-DIOXACYCLANES) AND THEIR ANALOGUES

Cyclic acetals play an important role in synthetic organic chemistry. The protection of vicinal hydroxy-groups of carbohydrates and sugars by acetal groups is widely known. The protection of the carbonyl group by the acetal group has been used successfully in the industrial synthesis of steroids and terpenoids.

Although 1,3-dioxacyclanes do not differ in principle in any way from open-chain acetals, nevertheless their cyclic structure is responsible for one characteristic feature which justifies the consideration of the reactions of 1,3-dioxacyclanes with OMC in a separate section. This feature is that 1,3-dioxacyclanes do not lose their oxygen-containing fragment on cleavage of the C–O bond by OMC in the way that open-chain acetals do.

As shown above, the exchange reactions of acyclic acetals with OMC have been investigated in fair detail. On the other hand, systematic studies on the analogous reactions of 1,3-dioxacyclanes began only recently. It appeared for a long time that 1,3-dioxacyclanes are fully resistant to the action of OMC. This was indicated by many facts. Thus 1,3-dioxolans with methyl substituents at $C_{(4)}$[44] or at $C_{(4)}$ and $C_{(5)}$[34] were suggested as solvents for Grignard syntheses. According to Nazarov[151], a bicyclic acetal with a complex structure, consisting of two 1,3-dioxolan fragments, does not react with OMC under the usual conditions. Many examples are known in which 1,3-dioxacyclanes containing functional groups react with OMC only via these functional groups without the cleavage of the C–O bonds in the acetal ring. In particular, the methylation of the terminal acetylenic group in 2-but-3-ynyl-2-methyl-1,3-dioxolan by ethylmagnesium bromide and methyl iodide in THF has been described[152]. The cleavage of the C–O bond has not been observed either in reactions of various carbonyl derivatives of 1,3-dioxolans with OMC[31,153-155].

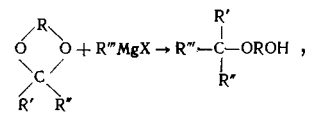
The interaction of 2-methoxy-1,3-dioxolans with OMC on heating leads to 2-alkyl(aryl)dioxolans[156]. The formation of OMC from cyclic five-membered acetals derived from saturated and unsaturated halogenoketones, including aromatic and heteroaromatic ketones, has been described[99,144,157].

The ethylene acetal of chloral is reduced by Grignard reagents to the dichloroacetaldehyde acetal in 74% yield[28].

When cyclic acetals of certain dihalogenoketones are treated with metallic magnesium, a three-membered ring is formed. The C–O bonds are not then affected[106]. All the data quoted above appear to have created a psychological barrier to studies on the cleavage of 1,3-dioxacyclanes by OMC. A few early studies[158-161] at the beginning of the century, in which the formation of the monoethyl ether of catechol from its formal on prolonged heating with methylmagnesium iodide was mentioned, were not developed further and were undeservedly essentially forgotten until the 1960's.

1. The Cleavage of 1,3-Dioxacyclanes by Grignard Reagents

Reactions involving the opening of the ring in various cyclic acetals by OMC [reaction (71)], leading to glycol monoethers (cellosolves), have been described almost simultaneously and independently by two research teams[2,34]:

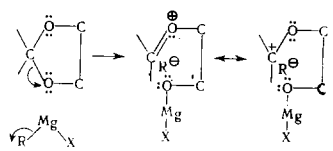


(71)

where R = $(CH_2)_2$, $(CH_3)CHCH_2$, $(CH_3)CHCH_2CH_2$, R′ = H, CH_3, or C_2H_5, R″ = H, C_2H_5, C_3H_7, or n-C_4H_9, R‴ = CH_3, C_2H_5, n-C_4H_9, C_6H_5, or CH_2=$CHCH_2$, and X = Br or I.

Cellosolves are usually obtained by the addition of alcohols to epoxyalkanes. The reaction is carried out in the presence of various catalysts[162] or by heating in an autoclave[163]. A mixture of ethers of mono-, di-, and tri-alkylene glycols, which are capable of interconversions under the reaction conditions, is as a rule formed[163]. The reaction of 1,3-dioxacyclanes with Grignard reagents made it possible to develop a fundamentally new method[5,6] for the preparation of a wide variety of glycol monoethers. The reaction is carried out at 60–130°C in solvents (benzene, toluene, or xylene) or in an excess of the acetal itself. The yield of hydroxyalkyl ethers depends on the structure and nature of the initial reactants, their proportions, the duration of heating, and the medium, reaching 82%.

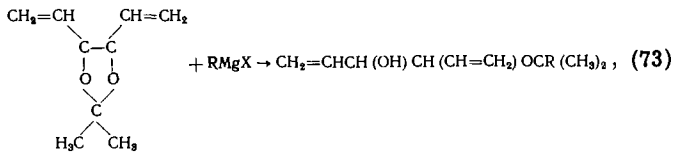
More than 30 different glycol monoethers obtained in this way have been described[22-24]. Cyclic formals are resistant to the action of Grignard reagents under the conditions investigated. As alkyl substituents accumulate in the 2-position, the reaction accelerates and the yield of cellosolves increases[22-24]. This behaviour is consistent with data for the influence of substituents on the hydrolysis[164,165] of 1,3-dioxacyclanes and also on their cleavage by halogenoacyls[166-170] and is probably due to similar causes: a change in electron density at the oxygen atoms which are the object of the primary electrophilic attack and in the stability of the intermediate carboxonium ion[24]. This finding conflicts with the concept of the primary nucleophilic attack on the $C_{(2)}$ atom, since under such conditions the electron-donating substituents in the 2-position should have retarded the process. The facilitation of the reaction with increase of the electron-donating capacity of substituents in the 2-position shows that the $C_{(2)}$–O bond dissociates before the formation of a new $C_{(2)}$–R bond (R is the group attached to OMC). The following mechanism has been proposed for the opening of the 1,3-dioxolan ring by OMC[34]:



(72)

According to mechanism (72), an increase in the electron-donating influence of the alkyl substituents in the 2-position should facilitate the cleavage of the acetal ring. The results of Blomberg at al.[34] indicate that ethylmagnesium bromide hardly reacts at room temperature with 2-methyl-1,3-dioxolan, while 2-ethyl- and 2-n-propyl-1,3-dioxolans form hydroxyethers under these conditions in yields of 39 and 78% respectively. The bulk of the alkyl groups in the Grignard reagent is reflected in the course of the reaction only when the dioxolan ring contains fairly bulky substituents[34]. The corresponding hydroxyethers have been obtained from the ethylene ketal of cyclohexanone on treatment with two equivalents of a Grignard

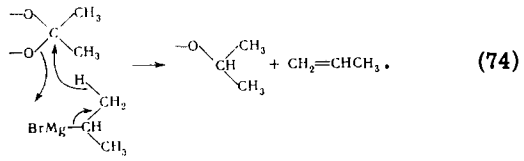
reagent in 91% yield (75°C, 16 h, benzene).[33] The reaction of 4-alkoxymethyl-2,2-dialkyl-1,3-dioxolans with ethylmagnesium bromide leads to the corresponding glycerol ethers[171]. The reactions of 2,2,4,4-substituted 1,3-dioxolans with various Grignard reagents [reactions (73)–(76)] have been described[29]‡:



(73)

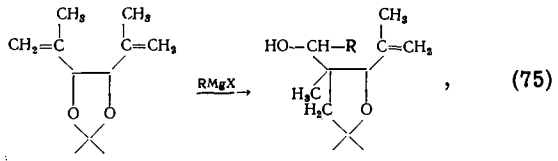
where R = CH_3 (X = I), C_2H_5, i-C_3H_7, or C_6H_5 (X = Br).

When R = i-C_3H_7, a reduction takes place:



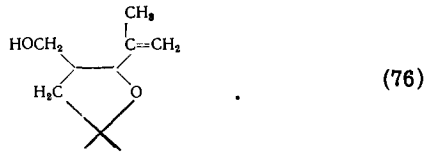
(74)

cis-Isomers undergo isomerisation:



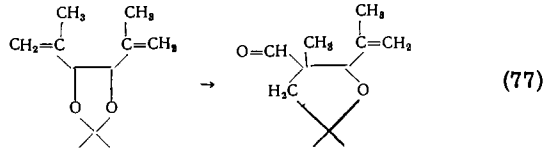
(75)

a primary alcohol being obtained with i-C_3H_7MgBr:



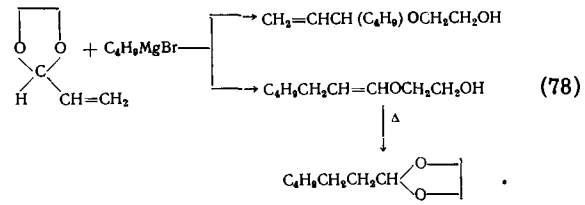
(76)

A rearrangement of similar acetals to furan aldehydes is known[173]:



(77)

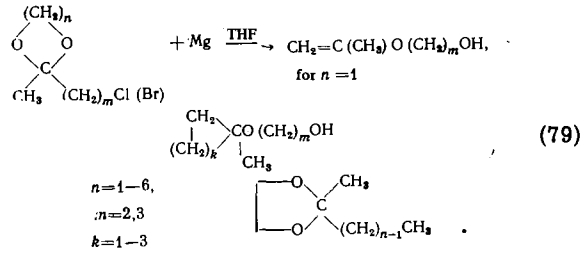
The latter are probably intermediates in the isomerisation described by Mousset[29]. When butylmagnesium bromide reacts with the cyclic acrolein acetal, the vinyl group is alkylated in addition to the normal mode of reaction [reaction (78)]. The process is accompanied by a prototropic rearrangement[130]:



(78)

‡ These problems are discussed in greater detail by Mousset[172].

The reactions of ω-halogenoalkyl-1,3-dioxolans with metallic magnesium have been considered[28,96,174]:

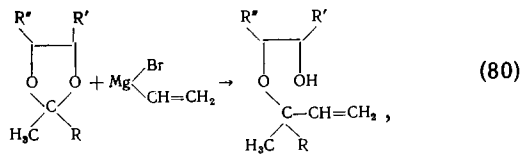


(79)

When $n = 3$, the formation of hydroxyethers is already accompanied by the reduction of the ω-halogenoalkyl substituent, which leads to the appearance in the reaction mixture of the corresponding 2-alkyl-2-methyl-1,3-dioxolans; when $n = 5$ or 6, the reduction becomes the only pathway followed in the process.

2. The Cleavage of 1,3-Dioxacyclanes by Vinylmagnesium Bromide and the Iotsich Reagent

Compared with saturated OMC, which readily rupture the C–O bonds of cyclic acetals and ketals, vinylmagnesium bromide is much less reactive in relation to these compounds[14]. Thus 2-ethyl-2-methyl-1,3-dioxolan begins to react with vinylmagnesium bromide only under relatively severe conditions (120°C, xylene):

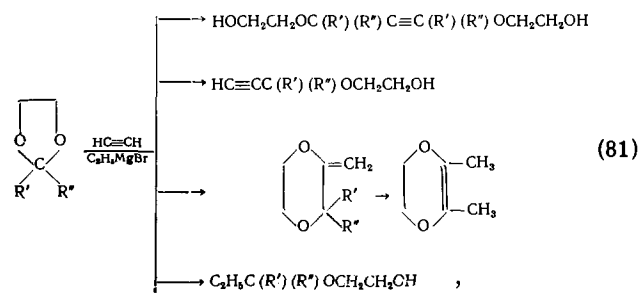


(80)

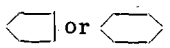
where R = H, C_2H_5, C_3H_7, or C_4H_9, R′ = CH_3, and R″ = CH_3.

β-Hydroxyalkyl ethers of ethylenic alcohols are obtained in yields of about 10%. 2-Butyl-2-methyl-, 2-ethyl-2,4-dimethyl-, and 2-ethyl-2,4,5-trimethyl-1,3-dioxolans were introduced into the reaction. Unsaturated β-hydroxyalkyl ethers could not be isolated in the case of 2-methyl- and 4-methyl-2-propyl-1,3-dioxolans, i.e. here too the conclusion that the reactivity of 1,3-dioxolans is reduced as the electron-donating properties of the substituents in the 2-position are weakened remains valid.

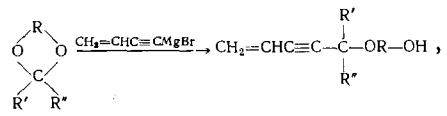
The cleavage of cyclic acetals by ethynylmagnesium bromide [reaction (81)] is accompanied by side reactions. A complex mixture containing, according to gas–liquid chromatographic and infrared spectroscopic data, various cyclisation products of the expected ethynyl ethers in addition to the ethers themselves as well as saturated hydroxyethers corresponding to the opening of the dioxolan ring by the initial Grignard reagent, is formed as a rule[19,22–24]:



(81)

where R′ = H or CH_3, R″ = CH_3 or C_2H_5, and R′,R″ =  or .

A number of hydroxyalkyl ethers derived from vinylethynylmethanols have been obtained in yields up to 80% by the reaction of various 1,3-dioxolans with vinylethynylmagnesium bromide (VEMB)[4,6,8,10,15,16]:



(82)

where R = $(CH_2)_2$ or $CH_2CH(CH_3)$, R′ = H or CH_3, and R″ = H, CH_3, C_2H_5, C_3H_7, or C_6H_{13}. In this process too the reactivity of 1,3-dioxolans increases somewhat with increase of the number and electron-donating capacity of substituents in the 2-position. Thus, whereas the yields of the hydroxyethyl ethers from 2-methyl- and 2-ethyl-2-methyl-1,3-dioxolans were 44.3 and 58.3% under comparable (but not optimal) conditions, unsubstituted 1,3-dioxolan could not be cleaved at all by VEMB.

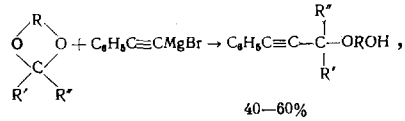
The introduction of the methyl group in the 4- or 5-position does not affect the reactivity of 1,3-dioxolan quite so significantly, although the latter is also apparently somewhat activated. One of the most important factors affecting the yields of hydroxyalkyl ethers derived from vinylethynyl alcohols is the reactant ratio[10] (see Table).

Variation of the yield of the vinyloxyethyl ether derived from methylvinylethynylmethanol with the initial reactant ratio.

Molar ratio 2-methyl-1,3-dioxolan : VEMB	Yield (w.r.t. VEMB), %
1:2	80
1:1	39.2
2:1	21.9

The yield of hydroxyethers depends no less significantly on the solvent. In ethyl ether the yield does not exceed 10%. When all the stages of the synthesis, including the preparation of the Grignard reagent, are carried out in the reacting acetal, it was possible to obtain the hydroxyether in yields up to 45%.[10] The effect of the halogen entering into the composition of the Iotsich complex on the yield of hydroxyethers has not been studied systematically. In the only relevant study[10] the use of $CH_2{=}CHC{\equiv}CMgI$ instead of VEMB (reactant ratio 1 : 1, benzene, 56–66°C, 2 h) was unsuccessful. The addition of catalytic amounts of $CoCl_2$ for an equimolar reactant ratio increases the yield to 57% compared with 39% (benzene, 80–90°C, 1.5 h). Higher $CoCl_2$ concentrations do not favour the reaction[10].

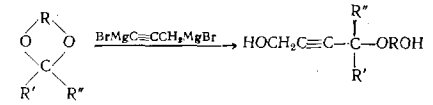
A number of β-hydroxyethyl ethers derived from secondary and tertiary phenyl-substituted acetylenic alcohols were obtained[7] from 1,3-dioxolans and phenylethynylmagnesium bromide:



40–60% (83)

where R = $(CH_2)_2$ or $(CH_2)_3$, R′ = H or CH_3, R″ = CH_3, C_2H_5, or C_3H_7, and R′ = R″ = . The reaction proceeds at 60–80°C. Iotsich complexes can be used under these conditions in the form of ether adducts with subsequent distillation of the ether, but they can be formed just as conveniently directly in the reacting cyclic acetal. To prevent the competing process, involving the saturated organomagnesium compound used to prepare the Iotsich complex, the intermediate Grignard reagent must then be synthesised at the lowest possible temperature (not above 40°C). Unsubstituted 1,3-dioxolan is resistant to the action of phenylethynylmagnesium bromide even at 100–120°C (xylene).

β-Hydroxyalkyl ethers of asymmetric acetylenic glycols were obtained by the reaction of certain 1,3-dioxolans with propynylenedimagnesium dibromide[3,24]:

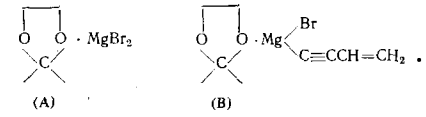


(84)

where R = $(CH_2)_2$ or $CH(CH_3)CH(CH_3)$, R′ = H or CH_3, and R″ = CH_3, C_2H_5, or C_3H_7.

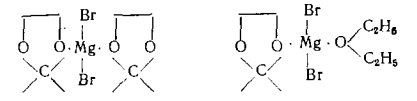
3. Complex Formation Processes

Like 1,4-dioxan, 1,3-dioxolans[175,176] can precipitate MgX_2 and RMgX from OMC solutions[8,10]. In the case of VEMB[8,10] the precipitate consists mainly of a mixture of the dioxolanates (A) and (B) in proportions of approximately 2 : 1:



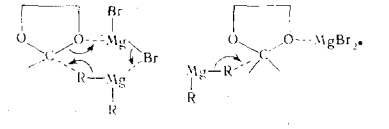
(A) (B) (85)

Small amounts of solvates of the type



(86)

were detected in the precipitate in addition to the complexes (A) and (B).[8,10] Thus ether adducts of Iotsich complexes probably have the same structure as the ether adducts of saturated magnesium halides and can be regarded as a mixture of $(CH_2{=}CHC{\equiv}C)_2Mg$ (40%), $MgBr_2$ (40%), and $CH_2{=}CHC{\equiv}CMgBr$ (20%). The reaction most probably proceeds via a synchronous electron transfer in cyclic or linear complexes[8,10]:



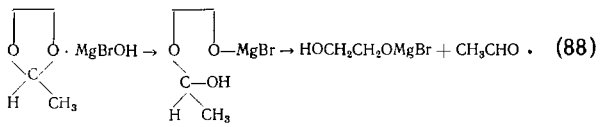
(87)

In such concerted nucleophilic substitution, the coordination O → $MgBr_2$ should play the most significant role. If the nucleophilic attack C_2 ← R were the most important factor, then electron-donating substituents at $C_{(2)}$ would hinder the reaction. The proposed mechanism gives a completely natural explanation of the requirement of at least a twofold excess of the Iotsich complex for the attainment of the maximum yield of hydroxyethers. A similar mechanism has been proposed for the cleavage of certain unsaturated acetals by OMC.[130]

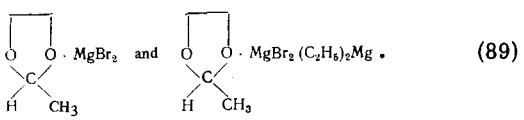
Insoluble complexes with certain 1,3-dioxolans are also formed by ethylmagnesium bromide. The principal components of the complexes are $MgBr_2$, C_2H_5MgBr, and

the corresponding dioxolan. The composition of the complexes is not constant and depends on the structure of the initial acetal, the reactant ratio, temperature, and the time of contact between the solid phase and the solution. It has been established for unsubstituted 1,3-dioxolan[10,11] that a decrease of temperature reduces the content of OMC in the precipitate. Gradual binding of 2-methyl-1,3-dioxolan by anhydrous $MgBr_2$ was observed[11]. The infrared spectrum of this complex hardly differs from that of the complex obtained from ethylmagnesium bromide at −20°C.

Basic magnesium salts are also capable of coordination interaction with cyclic acetals. However, the resulting complexes are unstable and tend to undergo further reactions (particularly on heating) with ring opening:

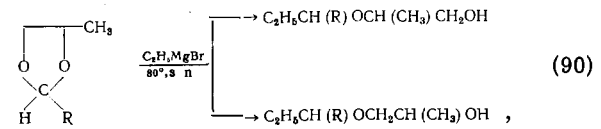

(88)

The rate of change of the OMC concentration in solution in the reaction between ethylmagnesium bromide and 2-methyl-1,3-dioxolan at 18°C has been measured[11]. The sharp decrease of the OMC concentration at the beginning of the reaction corresponds to the precipitation of the complex [the OMC concentration probably falls not only as a result of the binding of C_2H_5MgBr but also as a result of the adsorption of $(C_2H_5)_2Mg$ at the instant of the formation of the precipitate]; subsequently the OMC concentration over the precipitate changes much more slowly. Presumably the consumption of the OMC in this stage is due to the ring opening reaction itself. However, gas–liquid chromatographic analysis of the products of the hydrolysis of the reaction mixture failed to reveal even traces of the expected β-hydroxyethyl ether. The results correspond to the consecutive formation of complexes of two types:


(89)

4. The Mode of Cleavage of Asymmetrically Substituted 1,3-Dioxacyclanes

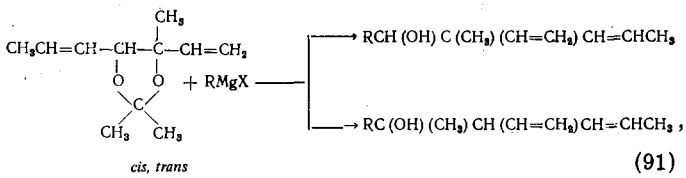
When 4-alkyl- and 2,4-dialkyl-1,3-dioxolans react with Grignard reagents[9], the products may be two structurally isomeric β-hydroxyalkyl ethers differing only by the position of the hydroxy-group—at the first carbon atom in one and at the second carbon atom in the other:


(90)

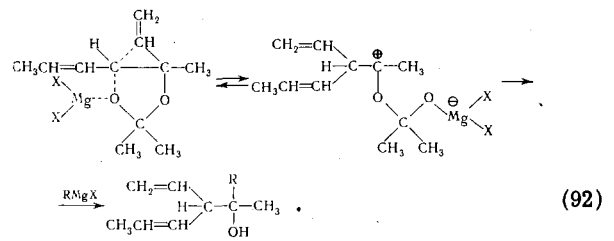
where R = CH_3 or C_3H_7.

However, it was found[9] that the reaction results in the almost exclusive formation of 2-hydroxy-1-methylethyl ethers. The admixture of the second isomer is slight, amounting to about 4% of the first.

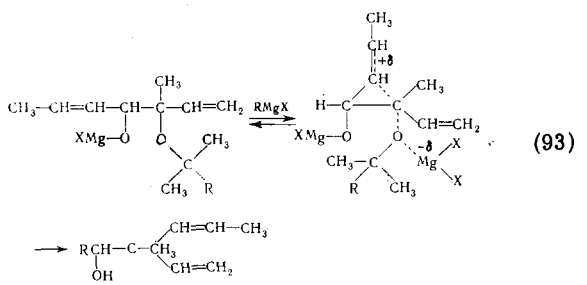
Interesting rearrangements were discovered[30] in the following reaction:


(91)

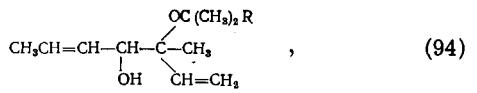
where R = CH_3 (X = I), C_2H_5, or C_6H_5 (X = Br). The formation of the tertiary alcohol begins with the rupture of the $O_{(1)}-C_{(5)}$ bond:


(92)

The cleavage of the $O_{(1)}-C_{(2)}$ bond leads to a secondary alcohol:

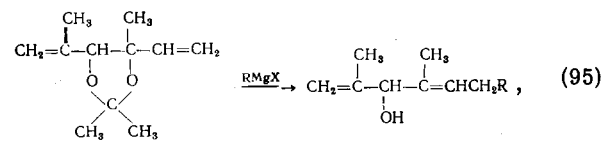

(93)

Thus both the tertiary and secondary alcohols are products of the attack by the OMC on the $O_{(1)}$ oxygen atom. The formation of hydroxyethers with the ether function at the tertiary carbon atom having the structure


(94)

which should have been obtained as a result of attack on the $O_{(3)}$ atom, was never observed in these reactions[30].

The cleavage of the C–O bond under the influence of a Grignard reagent in another 1,3-dioxolan with a structure very similar to that considered above was accompanied by the alkylation of one of the double bonds and its subsequent migration to the centre of the molecule[30]:

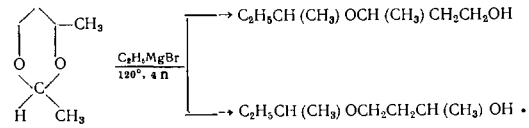

(95)

where R = CH_3 (X = I), C_2H_5, or C_6H_5 (X = Br).

The *cis*- and *trans*-isomers of 2,3-dimethyl and 4-methyl-2-propyl-1,3-dioxolans are cleaved by Grignard reagents at different rates[9]. The *cis*-isomers proved to be more reactive. This shows that the $O \rightarrow MgBr_2$ bond is oriented in space at a certain angle to the plane of the dioxolan ring, since otherwise the isomers of 2,4-dialkyl-1,3-dioxolans would be sterically indistinguishable in the formation of the intermediate complex[9]. These data, demonstrating a lower reactivity of 1,3-dioxolans with the

trans-disposition of the substituents with respect to the Grignard reagent, were subsequently confirmed in another study [30].

In contrast to asymmetrically substituted 1,3-dioxolans, 2,4-dimethyl-1,3-dioxan is cleaved by ethylmagnesium bromide with formation of two possible isomeric hydroxyethers in proportions of approximately 1 : 1 [17]:



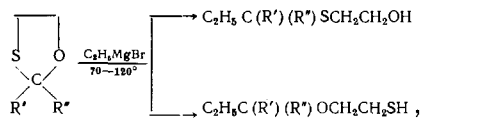
(96)

The change in the structural specificity of the cleavage of acetal rings on passing from five- to six-membered rings is associated with the conformations of the compounds. In contrast to the almost planar 1,3-dioxolans, 2,4-dimethyl-1,3-dioxan has the chair conformation with the *cis*-equatorial disposition of the CH_3 groups [17]. The 1 : 1 ratio of the isomeric hydroxyethers formed from this acetal shows that the *cis*-*e*,*e*-conformation to a large extent eliminates the steric hindrance to the interaction $O \rightarrow MgBr_2$, which is the initial stage in the cleavage of the 1,3-dioxacyclane.

However, the degree of structural specificity of the reaction depends on the bulk of the OMC molecules. When branched groups and bulky halogen atoms are present, the above effect of steric descreening of the $O_{(3)}$ atom in the 1,3-dioxan ring is insufficient for a preferential cleavage of the $O_{(1)} - C_{(2)}$ bond, of the kind observed in the cleavage of 2,4-dimethyl-1,3-dioxan by isobutylmagnesium bromide [17]. Thus the mode of cleavage of asymmetrically substituted 1,3-dioxolans and 1,3-dioxans is determined not only by the ring conformation but also to a similar extent by the steric characteristics of the OMC components [17].

5. The Cleavage of 1,3-Oxaheterocyclanes by OMC

1,3-Oxathiolans are cleaved by ethylmagnesium bromide with formation of 2-ethylthioethanols only [18,24]:

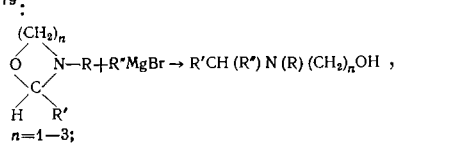


(97)

where R′ = H or CH_3 and R″ = H, CH_3, C_2H_5, or C_3H_7.

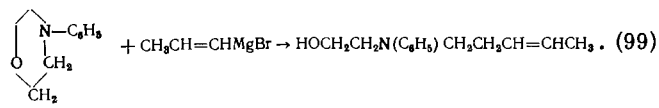
The unsubstituted ring is stable in the experimental temperature range (70–120°C). Compared with the corresponding 1,3-dioxolans, 1,3-oxathiolans are less reactive with respect to OMC [18]. Yet another feature of the reaction has been noted [18,23,24]: in contrast to 1,3-dioxolans, the introduction of two alkyl groups in the 2-position increases the stability of the 1,3-oxathiolan ring. 2-Monoalkyl-1,3-oxathiolans are the most reactive. This influence of substitution is evidence that in this instance the dissociation of the C–O bond does not precede appreciably the formation of the C–R bond, i.e. the reaction approaches the S_N2 type [18].

1,3-Oxazolidines are also cleaved by OMC at the C–O bond [115,177–179]:



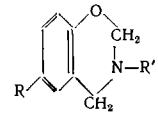
(98)

where R = H, CH_3, n-C_4H_9, i-C_4H_9, $(CH_3)_2CHCH_2$, or C_6H_5, R′ = H, CH_3, i-C_3H_7, or C_6H_5, and R″ = CH_3, $C_6H_5CH_2$, $(CH_3)_2CH$, CH_2=CH, or CH_3CH=CH_2. The yield of amino-alcohols reaches 80% in some cases. The reaction between 1,4-oxazolidines and propenylmagnesium bromide proceeds similarly [115]:



(99)

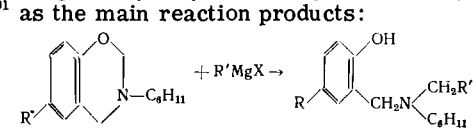
It has been found [180] that 2-oxazolidines of the type



(100)

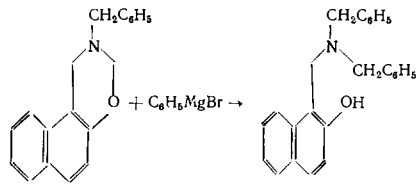
unsubstituted in the 2-position, do not react with CH_3MgI. However, later it was observed [181] that, when oxazines of similar structure are acted upon by a large excess of C_6H_5MgBr, the cleavage products are nevertheless formed in 8% yield.

When OMC interact with certain 1,3,2-dibenzoxazines, the benzoxazine ring is ruptured with formation of the corresponding 4-alkyl(aryl)-2-dialkylaminomethylphenols [74,101] as the main reaction products:



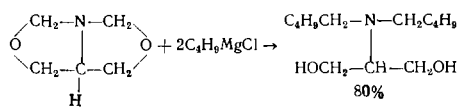
(101)

where R = $C(CH_3)_3$ or C_6H_5, R′ = CH_3, $(CH_3)_2CHCH_2$, C_6H_{11}, $C_6H_5CH_2$, or CH_2=$CHCH_2$ and X = Br, Cl, or I. The reaction is carried out in the presence of an excess of OMC. A similar reaction



(102)

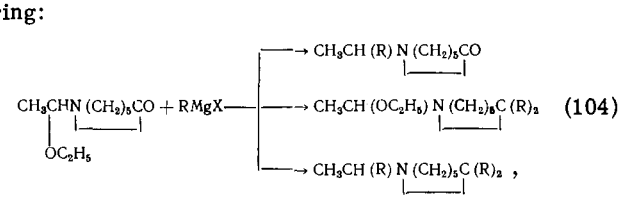
has been described [181]. The reaction



(103)

takes place at room temperature in the course of 24 h. [177]

N-(1-Ethoxyethyl)lactams [182,183] initially exchange preferentially the ethoxy-group for the group in the OMC and then the reaction involves the C=O bond with retention of the ring:

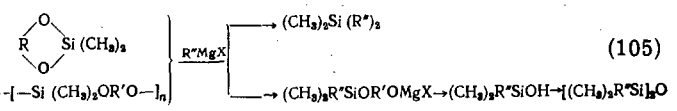


(104)

where R = C_3H_7, C_4H_9, or i-C_5H_{11} and X = Br.

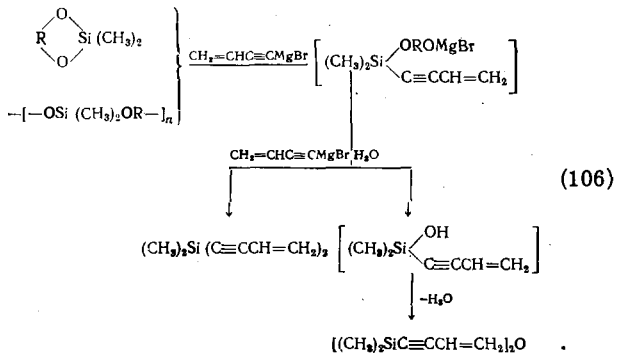
1,3-Dioxa-2-silacyclanes and their oligomers [20,25] readily undergo ring opening under the influence of alkyl-(aryl)magnesium halides at a temperature as low as 30–40°C with formation of trialkyl(diaryl)silylglycol monoethers. In addition, the second Si–O bond is also ruptured with formation of tetra-alkyl(trialkylaryl)silanes, whose yields increase in the presence of an excess of the

Grignard reagent and on raising the reaction temperature to 70–80°C:


(105)

where $R' = (CH_2)_2$, $(CH_2)_2O(OCH_2)_2$, or $(CH_2)_4$ and $R'' = C_6H_5$, C_3H_7, C_4H_9, or C_6H_5.

The cleavage of cyclic alkoxysilanes or the elementary units in the corresponding oligomers by VEMB proceeds as follows:[22,25]


(106)

The reaction occurs at 60–90°C. The above examples show that the Si–O bond is more reactive with respect to OMC than the C–O bond.

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Specific Complex Formation in Aqueous Solutions Involving Mononucleotides and Oligonucleotides

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Data on complex formation between synthetic polynucleotides and complementary oligo(mono)nucleotides are reviewed and analysed. The principal methods for the investigation of complexes are examined and the limits of their applicability are estimated. Attention is concentrated on the complex formation conditions (temperature, ionic strength, pH, concentration, component ratio, etc.). The influence of the nature of the heterocyclic base and the sugar and of the length of the oligonucleotide chain on the stoichiometry and thermal stability of the complexes is discussed.
The bibliography includes 150 references.

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I. INTRODUCTION

Numerous studies have been made in recent years on the interaction between complementary mononucleotides, oligonucleotides, and polynucleotides in connection with the expansion of research on the secondary structure of nucleic acids and on the relation between the structures of native macromolecules and their biological functions.

One of the approaches used to elucidate the causes and characteristics of the formation of involved native nucleotide complexes is based on the study of simpler synthetic systems. Recent studies have shown that such systems are convenient models for the investigation of many problems in molecular biology (codon–anticodon interactions[1], the problem of protein biosynthesis[2], DNA replication[3,4], etc.).

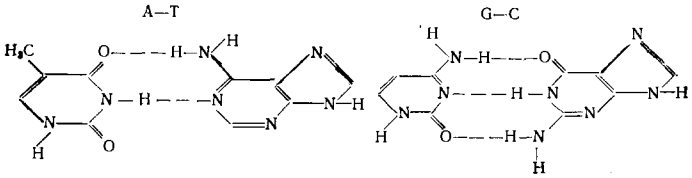
The study of the ability of mononucleotides, oligonucleotides, and polynucleotides to form DNA-like complexes in aqueous solution is also important from the standpoint of bio-organic chemistry in connection with the development of new approaches to non-enzymatic oligonucleotide synthesis on matrices[5-7].

Data published up to 1973 on specific interactions in simplest nucleotide systems are arranged systematically in the present review. Studies on monomer–polymer, oligomer–polymer and oligomer–oligomer complexes are considered, but problems of polynucleotide–polynucleotide interaction, which have been examined in a number of papers and monographs[8-10], as well as certain general problems such as theoretical consideration of the nature of the forces involved in complex formation[11-13] and the modern treatment of the "helix–coil" transition[14-16] are not discussed.

II. FUNDAMENTAL PRINCIPLES OF THE FORMATION OF OLIGOMER(MONOMER)–POLYMER AND OLIGOMER–OLIGOMER COMPLEXES

The capacity for the formation of specific intermolecular complexes in aqueous salt solutions is not characteristic solely of polynucleotides. It has been shown that short oligomers can also form under appropriate conditions ordered intermolecular structures with one another and with polymer molecules[17-25]. The formation of complexes by oligonucleotides and polynucleotides as well as native nucleic acid macromolecules is determined by three fundamental factors: the interaction of the heterocyclic bases (complementary and interplanar), the effect of the solvent, and the electrostatic effects of the phosphate groups.

Complementary (tranverse) interactions result in specific binding to one another of definite heterocyclic bases in adjacent polymeric (oligomeric) chains: adenine interacts with uracil (thymine) and guanine interacts with cytosine[26]:



The theoretical aspects of the problem of the stability of hydrogen-bonded pairs of bases are considered in the monograph of Kochetkov and Budovskii[10].

Interplanar longitudinal "stacking" interactions play an important role in creating a specific conformation of the mononucleotide, oligonucleotide, and polynucleotide chains involved in complex formation and ensure stability of the complex. By virtue of hydrophobic forces, the heterocyclic bases of each chain are arranged in a stack, in an attempt to avoid contact with water molecules; this is caused by the energy gain as a result of the entropy factor associated with the change in the number of structured water molecules around the dissolved substance when its molecules are associated to form a complex. Furthermore, the process is accompanied by a decrease in the surface tension energy due to the change in the surface area of the molecules on passing from the hydrated bases to their association complexes.

Using gel chromatography in conjunction with thermodynamic calculations, Bresler et al.[27] showed that the total

energy of the hydrogen bonds is much higher than the energy of the stacking interaction. On the other hand, it was believed previously that hydrogen bonds do not contribute significantly to the stabilisation of the complex[23].

Apart from the interaction between the bases and the influence of the solvent, the charges of the phosphate groups are an important factor. Whereas the binding of the heterocyclic bases to one another and to water molecules stabilises the complex, the repulsion of the negatively charged phosphate groups destabilises it.

A distinctive feature of the complexes considered in the present review is their marked dependence both on the overall concentration of the nucleotides and on the excess energy of the oligo(mono)nucleotide component in relation to the polymeric matrix[28]. A qualitative explanation of the latter has been given by Pitha and Ts'o[29] and by Uhlenbeck et al.[30] These workers showed that the local concentration of the monomeric units of two polynucleotides of comparable length in the interaction volume is fairly high. Under such conditions, the degree of complex formation is independent of the polymer concentration in solution.

On the other hand, when one of the chains forming the helix consists of mononucleotides or short oligonucleotides, the degree of complex formation is consistent with the law of mass action.

In an oligomer–polymer system the overall concentration of the oligonucleotide affects significantly its local concentration near the polymeric molecules and for this reason the degree of complex formation depends on the overall nucleotide concentration in accordance with the law of mass action.

In monomer–polymer systems the local concentration of the monomeric units is determined directly by the overall concentration of the monomer. Thus the concentration variation of the degree of complex formation in these systems should be most pronounced. The study of various oligonucleotide–polynucleotide complexes revealed a linear relation between $1/T\mathrm{m}$ and $\lg c$ (c is the concentration of the oligomer calculated in terms of the base and $T\mathrm{m}$ is the melting point)[28]. The slope of the experimental straight line depends on the length of the oligonucleotide chain. A general property of complementary complexes is the dependence of their stability on the ionic strength of the solution.

The contribution of electrostatic forces to the free energy of the "helix–coil" transition is specified by the equation[31]

$$\Delta E_{el} = RT(C_1 - C_2 \lg I),$$

where C_1 and C_2 are empirical constants and I is the ionic strength of the solution.

A linear relation between the melting point and $\lg I$ has been found for polymer–polymer systems[31,32]. It has been shown that the melting point of the complex increases with ionic strength. The same behaviour is characteristic of the oligo A-poly U system[33]. The stability of monomer–polymer complexes depends particularly strongly on the concentration of salts.

The presence of Mg^{2+} ions stabilises appreciably oligomer(monomer)–polymer complexes[34]. For example, an increase of the Mg^{2+} concentration in the $(pA)_4$–poly U system by a factor of 4 (from 10^{-3} M to 4×10^{-3} M) increases the melting point of the complex by 6.5 deg C.[35]

The most important property common to specific intermolecular complexes formed from both short and long nucleotide chains, is the cooperative nature of the decomposition of such structures, which is reflected in a comparatively narrow range of temperatures separating the ordered complex from the disrupted structure. At present the problem of the cooperative nature of the "helix–coil" transition is being solved within the framework of theories in which this process is considered from the standpoint of statistical physics. The essential feature of the cooperative transition is that its different stages do not occur independently but are interrelated and that the disruption of even one section of the helix leads to rapidly progressing breakdown of the entire structure. The cause of cooperative fusion is the breakdown of the interplanar interaction between pairs of bases[36]. The extent of the cooperative transition can be different for different systems and is characterised by the cooperativity factor $\sigma = e^{-E/RT}$, where E is the free energy of the stacking interaction of two isolated pairs of bases linked by hydrogen bonds.

1. Methods for the Investigation of the Complexes

The formation of helical nucleotide complexes in solution is accompanied by a significant change in their properties compared with those of the free components—an increase in molecular weight and rigidity of the structures, an increase in optical activity, the occurrence of hyperchromic and hypochromic effects in the absorption region, etc. This makes it possible to record and investigate the complexes by a number of physicochemical methods: infrared and ultraviolet spectroscopy[5,37], optical rotatory dispersion and circular dichroism[38,39], sedimentation analysis[40], viscometry[34], proton magnetic resonance (^{1}H NMR),[41] calorimetry[42], etc. In studies on oligomer–oligomer and oligomer(mono)–polymer systems optical methods are most widely used and these will be considered in somewhat greater detail.

Ultraviolet spectroscopy. Under complex formation conditions, the ultraviolet absorption intensity changes relative to the overall absorption intensity of the individual components. Depending on the wavelength of the absorbed light, the molar extinction coefficient of the complex can then be smaller (hypochromic effect) or greater (hyperchromic effect) than the sum of the corresponding extinction coefficients of the components or it can be equal to this sum. In the region of the absorption maximum the absorption intensity usually decreases on formation of the complex (Fig. 1). In certain cases where the initial components have an intrinsic secondary structure the formation of the intermolecular complex is accompanied by an increase in absorption[43].

The hypochromic effect is characterised by the percentage of hypochromicity ($\%h$) and reflects the degree of the stacking interaction between the bases in the complex. The temperature variation of the absorption of the solutions at a specified wavelength is usually determined by ultraviolet spectroscopy and the "melting" curves are plotted[9]. A number of thermodynamic characteristics can be calculated from the variation of the thermal stability of the complex ($T\mathrm{m}$) with the chain length of the oligomers and their concentration[33].

In the interaction between homo-oligonucleotides and polynucleotides the wavelength at which the molar extinction coefficient of the complex is equal to the sum of the extinction coefficients of the components serves as a characteristic from which one can infer the approximate

stoichiometry of the complex. The relation between the isochromatic wavelength and the stoichiometry of the complex was established by Stevens and Felsenfeld[44]. Subsequently Blake et al.[45] showed that this characteristic wavelength is 280 nm for 1A.1U double helices and 283.5 nm for the three-chain complex 1A.2U.

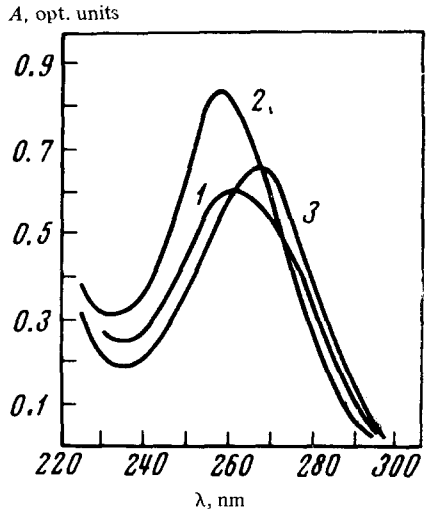


Figure 1. Ultraviolet spectra: 1) of the complex $A(pA)_7 \cdot d(pT)_8$; 2) of the component $A(pA)_7$; 3) of the component $d(pT)_8$ (9.4×10^{-6} M nucleotides, 1 M NaCl, pH 7.0, −5°C).[36]

Thus ultraviolet spectroscopy can yield all the necessary information about the interaction in the given system and its only disadvantage is that it is inconvenient for the investigation of solutions with a high concentration of nucleotides.

Optical rotatory dispersion (ORD) and circular dichroism (CD). In the formation of complexes of synthetic oligonucleotides and polynucleotides appreciable changes are observed in ORD and CD spectra: the shift of the 0–0 transition point to the short-wavelength region and the change in the amplitude of the Cotton effect[46–48]. The ORD or CD curve for the complex is usually compared with the overall curve obtained by adding together the curves for the individual components (taking into account their mole fractions in the complex) or with the ORD or CD curve for the mixture of the components at a temperature greater than the melting point of the complex. Useful information about complex formation is also provided by the "melting" curve reflecting the temperature variation of the molar ellipticity of the molar rotation measured at a specified wavelength. It is noteworthy that a hypsochromic shift of the ORD and CD spectra, a change in optical activity, and hypochromic effects in ultraviolet spectroscopy can be caused not only by the formation of specific complexes but also by the formation of various homoassociation.complexes. As a result, the experimental data for systems where a specific interaction is accompanied by the homoassociation of the components must be corrected[39].

Infrared spectroscopy. The stretching vibration wavenumbers of the NH_2, HN, and O=C< groups of the pyrimidine and purine bases change when these groups are involved in the formation of hydrogen bonds[49,50]. This is the basis of the method for the investigation of complex formation by infrared spectroscopy, whereby one can detect the occurrence of complementary interactions in the system.

The structure of the complex can be determined in two ways: (a) by comparing its infrared spectrum with that of a complex of known stoichiometry (the infrared spectra of polymer–polymer complexes with an appropriate nucleotide composition are usually employed as standards)[51]; (b) by measuring the variation of the intensity of the characteristic absorption band of the complex with mixture composition for a constant overall concentration of both components[10].

Infrared spectroscopy makes it possible to estimate quantitatively the degree of complex formation from the intensities of the bands appearing as a result of the interaction and the plot of this intensity against temperature constitutes the melting profile of the complex[52,53].

Infrared spectroscopy has many advantages over the methods discussed above. Since the infrared spectra of the individual components, their complexes, and self-aggregates as a rule differ from one another, this makes it possible to distinguish the interaction products and to infer the occurrence of non-specific interactions in this system[52]. An important advantage of the method is that it permits the employment of high nucleotide concentrations and complex formation can be studied under conditions which rule out the application of other optical methods. This is particularly valuable in the study of monomer–polymer systems where the concentration of the components plays a decisive role in the complex formation process[53]. A disadvantage of the method is the low intensity of the absorption bands arising as a result of the formation of hydrogen bonds.

2. The Stoichiometry of the Complexes

The most important characteristic of the complex is its stoichiometry. For synthetic homo-oligonucleotides and polynucleotides, there is a possibility of the formation, apart from the usual double helix, of a triple helix, the second polynucleotide (pyrimidine) chain being incorporated into the complex evidently via the formation of hydrogen bonds with the imidazole rings of the purine bases. Such structures are known for the A-U(T) pair in the crystalline state[54,55].

Studies in recent years showed that the stoichiometry of oligomer–polymer complexes is not determined unambiguously by the component ratio on mixing, but depends on a number of factors (temperature, ionic strength of the solution, bivalent metal ions, oligomer chain length, etc.).

The most common method for the determination of the stoichiometry of complexes involves the plotting of mixing curves (the so called Job method of continuous variations)[56]. For example, the ultraviolet absorption of mixtures containing different proportions of the reactants at a fixed overall concentration is measured and the optical density of the mixture is plotted against the mole fraction of one of the components. The extremum on the mixing curve indicates the stoichiometry of the complex. ORD,[57] CD,[48] and infrared spectroscopy[34] are also used to plot mixing curves.

The stoichiometric ratio of the bases interacting in the complex can be determined directly from the mole fraction of one of the components at which the extremum is observed:

$$r = \frac{(1-x)}{x},$$

where x is the mole fraction of one of the components and $1-x$ is the mole fraction of the other component.

When the extremum is broad, the stoichiometry of the complex is found by determining the point of intersection of the straight lines obtained by producing the linear sections of the mixing curve. However, when the curve is asymmetric (for example on formation of a three-chain complex) the extrapolation can lead to a gross error [58,59]. If self-aggregation of the components takes place in the system together with complex formation, additional terms taking into account the change in absorption and concentration due to self-aggregation, are introduced into Job's formula [47]. The calculation of the stoichiometric ratio is extremely difficult. In some cases it is possible to select the wavelength at which the self-aggregation process does not significantly influence the ultraviolet absorption of the system, whereupon the extremum on the mixing curve coincides with the maximum concentration of the complex, as in the absence of aggregation. For example, the stoichiometry of the complexes involving guanylic acid oligonucleotides is usually studied at 275 or 290 nm. [60]

The method based on mixing curves is used in the study of oligomer–oligomer and oligomer–polymer complexes. In the monomer–polymer interaction the complex formation depends very markedly on the concentration of the monomeric component, although in most cases there is no correlation between the component ratio in solution and the stoichiometry of the complexes [39]. The stoichiometry of the interaction is then determined directly by the ratio of the amount of monomer bound in the complex to the total amount of polymer in the solution (when the polymer molecules are completely bound in the complex). This ratio can be found by plotting the Ts'o isotherm [34] or the Scatchard diagram [61]. The interaction energy between nearest neighbours and the binding constant of the bases can be calculated from such graphs [62]. The stoichiometry of the complexes is also determined by viscometry, gel filtration [28], and equilibrium dialysis [63].

3. The Stability of the Complexes. Thermodynamic Parameters

The thermal stability of the complex is one of the main characteristics derivable directly from the experiment. Fig. 2 illustrates the thermal melting curve for the complex obtained by ultraviolet spectroscopy. If it is assumed that the optical density at a low temperature (below the plateau) corresponds to the completely helical structure and the optical density at the end of melting corresponds to the free components, then the proportion θ of the bases interacting in the complex can be calculated at any point in the transition range from the formula

$$\theta(t) = \frac{A_\infty - A_t}{A_\infty - A_0},$$

where A_∞ is the optical density of the solution of the fully denatured complex and A_0 is the optical density of the solution under optimal complex formation conditions.

The thermal stability of the complex is characterised by two parameters—the melting point (T_m) and the width of the transition range (ΔT_m) [64]. The melting point is the midpoint on the transition curve defined as the temperature at which the fractions of the helical and non-helical sections are equal, i.e. $\theta = 1/2$. For a given complex under constant external conditions, the melting point is constant. The width of the transition range is determined by the difference between the temperatures at which the tangent to the $(1-\theta)$–$t°$ fusion curve at the melting point intersects the lines corresponding to $1-\theta = 0$ and $1-\theta = 1$. ΔT_m reflects the cooperative nature of the transition, i.e. the degree of synchronisation of the breakdown of all the units of the helical structure with increase of temperature. For synthetic homopolynucleotides, the width of the transition range is related to the cooperativity factor σ as follows:

$$\Delta T_m = 12.4\, R \frac{T_m^2}{\Delta H} \sigma^{1/2},$$

where ΔH is the enthalpy of the transition.

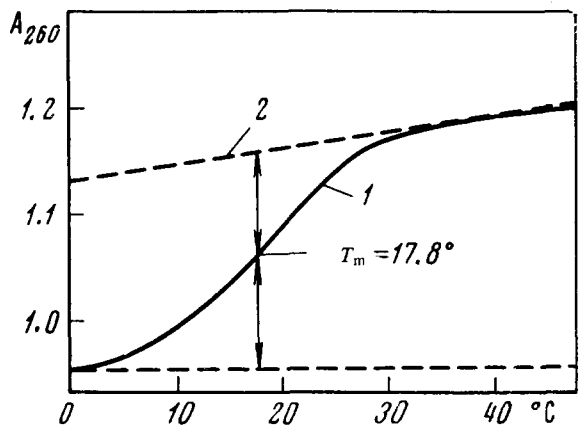


Figure 2. Temperature variation of the optical density A_{260} of the intermolecular complex $(Ap)_5U(pU)_4$ (1 M NaCl, pH 7.4): 1) experimental curve; 2) calculated absorption of the solution in the absence of interaction [63].

The theory of the cooperative "helix–coil" transition, developed in terms of modern statistical physics for polynucleotide models [65–67], is also applicable in the study of oligomer–oligomer and oligomer(monomer)–polymer interactions [68–72]. According to this theory, the first base pair formed in the oligomer–polymer (oligomer) interaction is much less stable than the subsequent pairs. The formation of each successive base pairs is associated with a specific stability constant, which rapidly approaches a limit in the transition range. It has been established that in most cases the differences between the stability constants of all the base pairs, other than the first, are insignificant and the cooperative transition can be described in terms of a model with two parameters.

Accordingly, the formation of a double oligomer–oligomer helix is represented schematically as follows:

$$A + B \overset{\beta S}{\underset{k_{10}}{\rightleftarrows}} D_1 \overset{S}{\underset{k_{21}}{\rightleftarrows}} D_2 \overset{S}{\underset{k_{32}}{\rightleftarrows}} \cdots \overset{S}{\underset{k_{N(N-1)}}{\rightleftarrows}} D_N,$$

where A and B are the interacting oligomers (oligomer and polymer), N is the length of the oligomer chain, D_i the partly helical structure with i pairs of bases, βS the stability constant of the first pair of bases, and S the stability constant of any of the succeeding pairs.

Statistical analysis of this scheme, taking into account the possibility of the existence of partly bound structures D_i, showed that β is extremely small ($\beta \ll 1$) and the constant S is very large ($S \gg 1$).[68-70] For relatively short oligomers, this makes it possible to neglect the concentrations of the partially bound structures $[D_i]$ and to treat complex formation in real systems in accordance with the "all or nothing" model:

$$A + B \overset{\beta S_N}{\rightleftarrows} D_N .$$

According to Applequist and Damle[68,69], this assumption does not introduce a significant error into the calculation of the thermodynamic parameters and ensures a simple quantitative relation between the thermodynamic parameters and the melting point, the slope of the fusion curve, length of the oligonucleotide, and its concentration in solution.

Table 1. Thermodynamic parameters of the "helix-coil" transition for a number of oligomer(monomer)–polymer systems[66].

Complex	Complex formation conditions	ΔH_1, kcal mole^{-1}	ΔS, kcal mole^{-1} deg^{-1}	β, mole^{-1}	Refs.
Poly U-adenosine (1A.2U)	D_2O; 0.15M NaCl, pD=7.0	−22.0	—	—	52
Poly U.2-amino-adenosine (1A.2U)	ditto	−22.2	—	—	52
Poly U-adenine (1A.2U)	»	−24.2	—	—	52
Poly U-2,6-diaminopurine (1A.2U)	»	−22.9	—	—	52
Poly C-5′-GMP (1G.2C)	D_2O; 0.2M NaCl, pD=7.0	−16.2	—	—	50
Poly U-oligo A (5′-phosphate)(1A.2U)	1M NaCl; 0.001M $MgCl_2$, pH 7.4	−14.4±3	−41.1±8	$0.1 \cdot 10^{1\pm1}$	35
Poly U-oligo A (3′-phosphate)(1A.2U)	ditto	−15.2±2.5	−43.7±7	$0.5 \cdot 10^{1\pm1}$	35
Poly U-oligo A (1A.2U)	0.1M NaCl; 0.01M $MgCl_2$, pH 7.0	−12.4±2.5	−38±7	$5 \cdot 10^{1\pm1}$	73
Poly U-oligo A (2′ → 5′)(1A.2U)	ditto	−11.6±3	−39±10	$1 \cdot 10^{2\pm1}$	73
Poly C-oligo G (1G.1C)	0.2M NaCl, pH 6.2	−7.0±3	−17.3±7	$1 \cdot 10^{1\pm0.5}$	74
Poly C-oligo I (1C.1I)	0.01M $MgCl_2$; pH 7.0	−6.2±0.3	−17.4		75

To simplify the calculations, it is assumed that ΔH_1 and ΔS_1 (the molar enthalpy and entropy of formation of a pair of bases), are the same for all the pairs and that β is independent of temperature. Then the enthalpy and entropy of the transition are proportional to the oligomer chain length:

$$\Delta H = N\Delta H_1, \quad \Delta S = N\Delta S_1 .$$

Damle[70] calculated a number of thermodynamic parameters for several oligomer(monomer)–polymer systems from the experimental data of other investigators. The results of these calculations are presented in Table 1.

A monomer–polymer system, for which thermodynamic calculations can be made even when the monomers are aggregated in solution, constitutes a real system most closely corresponding to the "all or nothing" model[71].

Later investigations of a number of oligomer–oligomer complexes showed that in real systems β is a function of temperature and the enthalpy of formation of the first base pair is significantly different from the molar enthalpy of formation of the subsequent pairs[36,71,76-78]. Thus, although the simplified theory of Applequist and Damle does in fact make it possible to estimate to a first approximation the thermodynamic characteristics of complex formation in the system as a whole, it does not reflect quite correctly the thermodynamics of the individual stages of this process.

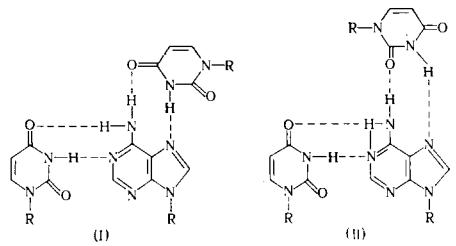
III. COMPLEXES OF MONOMERS WIT H POLYNUCLEOTIDES

The formation of complexes of monomers with complementary polynucleotide with rigorous structural specificity has been observed for only one combination of components: a purine monomer and a pyrimidine polymer[34,39,41,50,53]. It has not so far been possible to obtain the corresponding complexes involving pyrimidine monomers[50]. This is probably because the smaller surface area of the pyrimidine base compared with that of the purine base leads to a smaller degree of their overlapping in the formation of a pseudopolymeric structure in the complex and therefore to a lower stabilisation of the complex via the stacking interactions of the covalently non-bonded monomers. For this reason, such complexes should be significantly less stable, if they are formed at all, than the complexes of purine monomers.

A characteristic feature of the monomer–polymer complexes is their marked dependence on the concentration of the monomeric component. The polymer concentration does not actually influence the stability of the complexes—a tenfold increase of the amount of poly U did not affect the stability of the poly U-2-aminoadenine system[63].

Stoichiometry of monomer–polymer complexes. Among the monomer–polymer systems, the interactions of adenosine or its derivatives with 2 poly U have been most widely investigated[34,50,78-80]. Whereas oligomer–polymer or polymer–polymer systems lead to the formation of double and triple helical structures[28], the formation of triple-stranded complexes consisting of two polynucleotide chains and one pseudopolymeric chain formed by the monomers is prefered in the monomer–polymer interaction. The stoichiometry of these complexes (1Pu-2Py) can probably be accounted for by the thermodynamics of the complex formation process. The formation of an ordered secondary structure is as a rule associated with a decrease of entropy which is unfavourable for the process. In this case the heat of reaction should provide the driving force for the process. According to the results of Ross and Scruggs[81], the formation of a triple-stranded complex involving the monomer is accompanied by a large entropy change (about −42 cal mole^{-1} deg^{-1}) compared with the entropy of formation of the triple polymer–polymer helix (about −32 cal mole^{-1} deg^{-1}). Evidently the heat of formation of the double-stranded complex is insufficient to compensate such a high entropy change and in a monomer–polymer system the addition of another chain, which ensures a further enthalpy gain, is necessary. The authors attribute the differences between the entropies of formation of monomer–polymer and polymer–polymer complexes to a greater degree of disorder in the monomer in solution compared with the rigid molecules of polynucleotides. Felsenfeld and Miles[53]

proposed two possible structures for the monomer–polymer complexes A.2U, differing in the disposition of the poly U chains: the chains are antiparallel and parallel in the first and second structures respectively (see below).



(I) (II)

Both structures satisfy the requirements of stoichiometry. However, the study of the infrared spectra of the complex A.2poly U showed that the poly U chains are linked to the adenine residues by different carbonyl oxygen atoms[37]: one of the chains forms pairs of hydrogen bonds via $-C_{(4)}=O$ and $N_{(3)}-H$ and the other via $-C_{(2)}=O$ and $N_{(3)}-H$. This finding supports structure (II), in which the second polynucleotide chain is linked to the adenine bases in accordance with the scheme of Haschemeyer and Sobel[55].

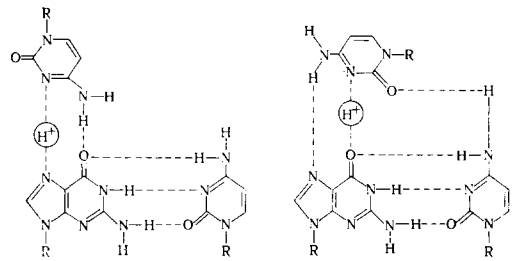
The structure with the antiparallel disposition of chains is also entirely likely for the monomer–polymer complex. In this complex the polynucleotide chains can belong to the same poly U molecule folded in two and are linked to one another via the adenine monomers.

On the basis of the results of sedimentation analysis, Huang and Ts'o[34] suggested the formation of a double-stranded complex of adenosine with poly U at 20°C. However, this conclusion was not confirmed by CD [79] and equilibrium dialysis[63] studies on the system. Damle[80] believes that the triple-stranded complexes 1A.2poly U constitute the only form of interaction between adenosine and poly U regardless of the concentrations of the components and temperature. It should also be noted that the infrared spectra and the melting curves obtained by Howard et al.[50] indicate the complete dissociation of the triple-stranded complex, $A.U_2 = A + 2U$, without the intermediate formation of the complex 1A.1U, The formation of the complex 1A.1U instead of 1A.2U should be reflected in a change in the infrared spectra—the appearance of an intense absorption band at 1672 cm^{-1}, while the 1657 cm^{-1} band is characteristic of the 1A.2U structure[53].

As a result of the presence of substituents in the purine base in the positions responsible for the binding of the second polynucleotide chain, the complex either does not form at all (for example in the case of tebericidin) or a very high concentration of the reactants is required. Thus Huang and Ts'o[34] failed to detect the formation of the complex of $N_{(6)}$-methyladenosine and poly U. On the other hand, Howard et al.[50] discovered the formation of a 1 : 1 complex of 9-methyl-6-methylaminopurine with poly U after increasing the concentration of the reactants.

The interaction of guanine monomers with poly C depends to a large extent on the pH of the solution. Thus at pH 7.8, where the protonation of poly C is impossible, guanosine 5'-phosphate forms the complex 1G.1C with poly C.[52] In the range pH ≤ 7, the complex has the structure 1G.2C, although in this case the formation of a triple-stranded helix requires the presence of the protonated form of poly C^+ at a fairly high pH. However, potentiometric titration has shown that the protonation of polycytidylic acid is facilitated in the present of guanosine, the pK of poly C being displaced towards the neutral region[39].

Among all the schemes proposed at present for the binding of 1G.2C,[74,79] most workers give preference to structure (A) (see below).



(A) (B)

One should note that melting of the triple-stranded complexes 1G.2C takes place in different ways in neutral and acid solutions[39]. At pH 6.4 the complex decomposes to the initial components as the temperature increases, while at pH 4.5, the guanine monomers are "melted out" and the double-stranded structure of poly C and poly C^+ remains. Such denaturation of the complex is more likely for structure (B), in which the parallel poly C and poly C^+ chains are linked. Evidently one can not rule out the possibility that different structures exist at different pH.

The study of the role of substituents in the heterocyclic ring of the purine component involves in most cases attempts to a quantitative estimation of the individual contributions of hydrogen bonds to the stabilisation of the complex. Evidently the contributions to the interaction energy due to other forces involved in the formation of the structure also vary on formation of a new hydrogen bond. For this reason, it is sometimes difficult to determine the main cause of stabilisation[42,50].

It has been observed that the introduction of substituents in the 1-, 6-, and 7-positions prevents the interaction of the monomer with the corresponding polynucleotide[34,39,82–84] Thus $N_{(1)}$-methyladenosine, where the introduction of the methyl group effects simultaneously the two sections responsible for the binding, is incapable of interacting with poly U.[42,50] Sarocchi et al.[39] also note that poly C does not form a complex when guanosine is replaced by 7-methylguanosine, 6-chlororibosylpurine, 6-thioguanosine and 2,6-diaminoribosylpurine.

Howard et al.[50] observed that complexes of 2-aminoadenosine and 2-aminoadenosine 5'-phosphate with poly U are more stable than the corresponding complexes of adenosine and 5'-AMP. The 2-amino-group participates in the formation of an additional hydrogen bond with one of the poly U chains, which results in the formation of a system resembling 1G.2C. The stoichiometric formula of the complexes of 2-aminoadenosine with poly U is 1A.2U.[63]

Substituents which do not prevent the formation of hydrogen bonds have hardly any influence on the capacity of the monomer for complex formation and on the stability of the complex. For example, the stability of complexes of poly U with various 3- and 9-alkyl-substituted adenines is close to that of complexes with unmodified adenine[34]. The formation of a complex of poly U with 8-aza-2,6-diaminopurine instead of adenine has been observed[50].

The sugar residue in the monomer molecule is not involved in the formation of the sugar phosphate skeleton which strengthens the chain, as happens in polynucleotides. For this reason, the replacement of the purine base by the appropriate nucleoside does not as a rule have a significant

influence on the stability of the complex, although Ts'o noted in a number of cases some stabilisation by the carbohydrate group. The nature of the sugar residue (ribose or deoxyribose) and its configuration (D- or L-ribose) is apparently unimportant at the level of monomer–polymer interactions[34]. A comparative study has been made of a number of systems of homopolymers and copolymers (poly AC, poly UC, poly UG) with monomers by equilibrium dialysis in combination with ultraviolet spectroscopy[63]. The authors established that the copolymer systems obey the same relations as the homopolymer systems. The employment of a mixture of monomers made it possible to compare the strength of the complementary interaction of individual monomers. For example, a study of the formation of complexes by poly UC with a mixture of dG and dA or dG and 2-aminoadenosine revealed a greater degree of binding in the second case.

Effect of the terminal phosphate group. Complexes of mononucleotides with polynucleotides have been least thoroughly investigated among the monomer–polymer systems, although they are of considerable interest from the biological point of view.

The first study in which mononucleotides were detected and investigated was carried out by Howard et al.[82] At high nucleotide concentrations (0.10–0.25 M) the presence of double- and triple-stranded structures, formed by guanylic acid mononucleotides (5'-GMP and 5'-dGMP) with polycytidylic acid, was established by infrared spectroscopy. It was noted that at pD 7.8 the infrared spectrum of the complexes is similar to that of the complex GpGpGp. .poly C, the stoichiometric formula of which is 1G.1C according to Lipsett[74]. At pD ≤ 7 new absorption bands appeared in the spectra of the mononucleotide–polynucleotide complexes, indicating the formation of triple-stranded helices containing the protonated form poly C^+.

Guanylic acid monomers, which are known to show a tendency towards self-aggregation and the formation of gels, sometimes precipitate from a nucleotide concentration of 0.01 M even in solutions at low ionic strength[39]. It is extremely likely that at this high nucleotide concentration the investigators observed the interaction between poly C and complex guanylic acid gels. Sarocchi et al.[39] investigated mixtures of guanylic acids with poly C in weakly acid dilute (overall nucleotide concentration 0.002 M) solutions. The formation of the complex 1G.2C noted under these conditions depends on the pH of the solution: complex formation was observed only at pH ≤ 6. In all probability this upper pH limit to the stability of the complexes is caused not only by the necessity for the protonation of poly C to form a triple-stranded complex but also by the need to suppress the dissociation of the secondary phosphate groups of the mononucleotide. The difference in the behaviour of the complexes of 5'-GMP and 3'(2')-GMP with poly C merits special attention: the latter complex is stable over a wider pH range. Guanylic acids with a phosphate group in the 5'- or 3'(2')-position are known to exhibit different tendencies towards self-aggregation and form gels of different structures[85–87]. However, the differences between their complexes with poly C have not so far been explained.

The study of Ts'o and Huang[40] occupies a special place among those dealing with the interaction of nucleoside mono-, di-, and tri-phosphates with polynucleotides. In solutions with a moderate concentration of the components in the presence of $MgCl_2$ the authors observed that the formation of complexes by purine nucleotides with the corresponding polynucleotides entails the precipitation of the complex. It was not possible to detect complexes in the supernatant. On the basis of these observations, the authors suggested that complex formation of mononucleotide–polynucleotide systems requires an additional driving force, which may be a phase transition. Complexes of monomer triphosphates proved to be less stable than complexes of monophosphates. Studies on the formation of complexes by cyclophosphates[88] showed that they give rise to more stable complexes with polymers than nucleotides. This can probably be explained by the decrease of the charge of the phosphate, which is particularly important for mononucleotides. The conditions governing the complex formation and the characteristics of a number of monomer–polymer complexes are given in Tables 2 and 3.

Table 2. The interaction of purine bases and nucleosides with polynucleotides.

Monomer	Polynucleotide	Conc., M: of monomer	Conc., M: of polymer	Complex formation conditions	Stoichiometry of complex	M.p. of complex, °C	References
Adenosine	Poly U	0.015	0.030	0.15*M* NaCl	1A·2U	18.5	50
ditto	ditto	0.030	0.015	0.6*M* NaCl, pH 6.9	1A·2U	—	42
»	»	0.015	$0.925\cdot10^{-2}$	0.1*M* NaCl	1A·2U (5°)	11	34
»	»	0.015	$0.925\cdot10^{-2}$	0.4*M* NaCl	1A·1U (20°)	18	34
»	»	0.015	$0.925\cdot10^{-2}$	0.02*M* $MgCl_2$		31	34
»	»	$0.5\cdot10^{-3}$	$3.6\cdot10^{-3}$	1*M* NaCl+0.01*M* $MgCl_2$ + 0.01 M Na cacodylate; pH 6.97		—	80
»	»	$12\cdot10^{-3}$	$3.6\cdot10^{-3}$	0.1*M* NaCl+0.01 M Na cacodylate; pH 6.97	1A·2U	—	80
D-Adenosine	»	0.015	0.030	0.15*M* NaCl	1A·2U	18.5	50
L-Adenosine	»	0.015	$0.925\cdot10^{-2}$	0.02*M* NaCl	1A·2U		34
2-Amino-adenosine	»	0.015	0.030	0.15*M* NaCl pH 6.9	1A·2U	31	42
ditto	»	0.034	0.030	0.125*M* NaCl, pH 6.9	1A·2U	36	42
»	»	0.030	0.015	0.6*M* NaCl, pH 6.9	1A·2U	47.7	42
8-Aza-2,6-diamino-purine	»	0.015	0.030	0.14*M* NaCl	1Pu·2U	—	50
»	»	0.067	0.100	0.15*M* NaCl	1A·2U	24	50
Adenine	»	0.045	0.090	0.15*M* NaCl	1A·2U	44	50
2,6-Diamino purine	Poly C	0.034	0.0688	0.125 M Na cacodylate; pH 6.9	1G·2C	36	50
Guanosine	ditto	$1.38\cdot10^{-3}$	$0.75\cdot10^{-3}$	0.2 M Na cacodylate; pH 6.7	1G·2C	—	39

Analysis of studies of the dependence of monomer–polymer systems on the monomer concentration leads to the conclusion that the interaction requires a definite minimum monomer concentration (the "lower threshold"), which depends on the nature of the monomer, the pH of the solution, ionic strength, and the presence of Mg^{2+} ions. On further increase of the monomer concentration, the thermal stability of the complexes rises, but, after the attainment of a concentration characteristic of the given conditions, saturation takes place, the degree of complex formation reaching a limit and not changing further. Graphically the process can be represented by the Ts'o isotherm[39]. According to Huang and Ts'o, the existence of the "lower concentration threshold" can be accounted for by the fact that the interaction of monomers with polymers is preceded by the self-association of the monomeric molecules in solution:

$$nM \rightleftarrows M_n,$$

where M is the monomer molecule and n the number of monomeric units in the aggregate ($n = 1, 2, 3, \ldots$).

The aggregates formed (stacks) then interact with the polymer to form the corresponding complexes. The formation of the stacks initiates the complex formation process and determines the minimum monomer concentration in solution.

Table 3. The interaction of nucleoside phosphates with polynucleotides.

Monomer	Polynucleotide	Concn., M		Complex formation conditions	Stoichiometry of complex	M.p. of complex, °C	Refs.
		of monomer	of polymer				
5′-AMP	Poly U	0.026	0.050	0.075*M* $MgCl_2$,	1A·2U	14	51
ditto	ditto	0.010	0.010	0.03*M* $MgCl_2$, pH 5.8	1A·2U complex in ppt		40
2-NH_2-5′-AMP	»	0.030	0.060	0.18*M* NaCl	1A·2U	11	50
5′-ATP	»	0.020	0.010	0.08*M* $MgCl_2$	1A·2U	11	51
5′-dATP (or 5′-ATP)	»	0.020	0.010	0.04*M* $MgCl_2$, pH 7.0	1A·2U complex in ppt		40
5′-GMP	Poly C	0.054	0.109	*pD* 7.0	1G·2C	~23	52
ditto	ditto	0.115	0.115	*pD* 7.8	1G·1C	~15	52
»	»	0.010	0.010	0.04*M* $MgCl_2$ pH 7.0	1G·1C complex in ppt		40
»	»	$0.16 \cdot 10^{-2}$	$0.1 \cdot 10^{-2}$	1*M* NaCl, pH 5.3–5.6	1G·2C		39
2′(3′)-GMP	»	$0.2 \cdot 10^{-2}$	$0.1 \cdot 10^{-2}$	1*M* NaCl, pH 3.0–6.0	1G·2C		39
5′-GTP	»	0.02	0.04	0.04*M* $MgCl_2$, *pD* 6.1	1G·2C	25	51
ditto	»	0.02	0.01	0.08*M* $MgCl_2$, pH 7.0	1G·1C complex in ppt		40
»	»	0.02	0.04	0.08*M* $MgCl_2$, pH 7.0	1G·2C complex in ppt		40

There exists also another point of view. Felsenfeld and Miles [53] believe that the self-aggregation of monomers must be regarded as a process competing with specific complex formation. The mutual orientations of the purines in the stacks and in an ordered complex are probably different, since in the former case the orientation is determined mainly by the hydrophobic interaction of the aromatic rings and in the second by the action of stereospecific forces. Since there is no rigorous mutual orientation of the monomers in the stacks (this is indicated by the ORD and CD spectra of the monomer solutions), the interaction of the stacks with the polynucleotide should involve their decomposition and the rearrangement of the monomers in accordance with the stereochemical requirements of the helix.

There is at present no reliable information about the involvement of the monomer–polymer complexes in natural biological processes. However, the inhibition of the peptide synthesis directed by the polynucleotide matrix in a cell-free system in the presence of complementary monomers, observed by Maxwell et al. [2], suggests that the monomer–polymer interactions can control the transfer of genetic information in the cell. Such control can occur at different levels of information transfer—in both transcription and translation stages.

IV. COMPLEXES OF OLIGONUCLEOTIDES WITH POLYNUCLEOTIDES

Oligomer–polymer complexes are more stable than the monomer–polymer complexes, which makes it possible to use them as convenient models for the investigation of complex formation. Oligomers containing not only purine bases (as happens in monomer–polymer interactions) but also pyrimidine bases [3,34,81,89] take part in the complex formation process. The structures and physical properties of the oligomer–polymer complexes are close to those of the polymer–polymer association complexes.

The stoichiometry of the A—U(T) complexes is not determined unambiguously by the component ratio in solution, but does depend on a number of factors, one of which is the nature of the oligonucleotide. Thus, according to Cassani and Bollum [28], at a moderate ionic strength the oligomers of thymidylic acid forms a complex 1T.1A with poly dA even in the presence of Mg^{2+}, while the structure 1A.2T is produced in the system of short dA oligomers and poly dT. The reason for the different stoichiometries is probably that in the 1Pu.2Py triple helix, formed with participation of oligo dA, there are breaks in the adenylic acid chain alone. In the triple-stranded complex oligo dT–poly dA, two chains of the helix consist of oligomers. Other conditions being equal, the stability of the latter complex should be much lower than that of the former [81].

The effect of the nature of the sugar residue on the structure of the polynucleotide chains and helices has been discussed in the literature for several years [90–95]. Marked differences have been observed between the CD spectra of the complexes poly-(A-A-U).poly-(A–U-U) and their deoxy-analogues, which may be due to the difference between their carbohydrate components [91].

It has been shown for polymer–polymer systems that the stability of the complexes of deoxypolynucleotides and mixed complexes is lower than that of the corresponding ribopolynucleotide systems [90]. The same behaviour is observed for oligomer–polymer complexes, the nature of the sugar residue of the polynucleotide component playing a particularly important role. The two-chain structure characteristic of the complex $d(pT)_{10}$.poly dA gives way to a triple-stranded structure when poly dA is replaced by polyrA (Fig. 3). [28]

Possibly the role of the 2′-OH group in the stabilisation of the triple-stranded helix is associated with the formation of additional hydrogen bonds in which the hydroxy-group can be involved as a proton acceptor [92] or donor [93]. Ts'o et al. [94] suggest the formation of intramolecular hydrogen bonds between 2′-OH and the $N_{(3)}$ atom of purine, the $O_{(2)}$ atom of pyrimidine, or the phosphate group. However it is still not clear how this can promote the introduction of a second polynucleotide chain into the complex.

A number of other investigators [90,92] suggested that the effect of the 2′-OH group on the structure and stabilisation of the helices is due to a change in the conformation of the sugar ring and the interaction of the ribose 2′-hydroxyl with solvent molecules. There is as yet no sufficiently convincing evidence in favour of a particular point of view.

By varying the chain length of the oligonucleotide in the system d(pA)m–poly dT, it has been shown that there is a critical value of m (characteristic of the given ionic strength of the solution) at which the interaction of an equimolar mixture of the oligomer and a polymer begins to form a double-stranded complex [28]. The formation of

a triple-stranded helix is characteristic of all oligo dA whose length is smaller than this value, regardless of the component ratio in solution. The authors noted that, near the critical value of m-, an equilibrium is established in the equimolar mixture of the components between the double- and triple-stranded complexes: there is a two-stage melting curve, the optical density at 260 nm in the first fusion stage and the decrease of the optical density at 284 nm being due to the complex 1A.1T, while the optical density at 260 nm in the second fusion stage indicates the decomposition of the complex 1A.2T (Fig. 4). A true equilibrium is probably observed in the system: the ratio of the double- and triple-stranded complexes did not change even on incubating the solution (5°C) for three months.

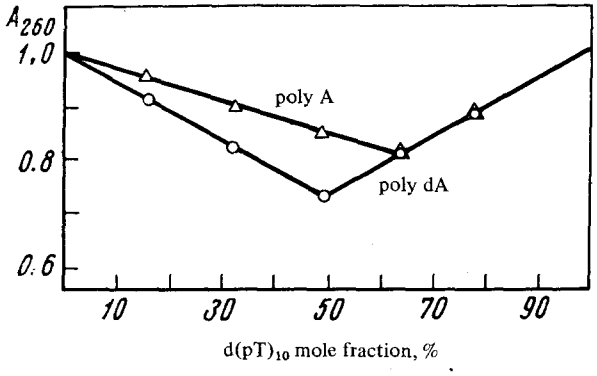


Figure 3. Mixing curves for complexes of $d(pT)_{10}$ with poly A and of $d(pT)_{10}$ with poly dA (1 M NaCl, pH 6.8, 23°C).[28]

As in the interaction of polynucleotides[96,97], an increase in ionic strength promotes the formation of triple-stranded oligomer–polymer helices. Thus Rich[89] observed a change in the stoichiometry of the two-helix oligo dT. .poly A complex and the formation of a triple-stranded structure with increase of the concentration of LiCl. Certain bivalent metal ions play an even more effective role in the stabilisation of triple-stranded complexes. For example, in order to obtain the complex 1A.2U in the system $(pA)_4$–poly U, the 1 M NaCl solution can be replaced by 0.001 M magnesium chloride solution[35]. The main function of the salts introduced into the solution is to shield the charged phosphate groups of oligo- and polynucleotides. The greater effectiveness of bivalent cations compared with univalent cations is a consequence, according to Michelson[9], of the differences between the dissociation constants of the corresponding metal phosphate salts. One cannot rule out the possibility that polyvalent cations can bind simultaneously the phosphate groups in different chains, which should also promote the formation of triple-stranded complexes.

The influence of ionic strength and bivalent metal ions on the interaction of polyanions such as oligo- and polynucleotides is very great. This factor sometimes plays a decisive role in the formation of the complex and with the given stoichiometry. Thus the interaction of oligo A with poly U in the presence of Mg^{2+} leads to the formation of the triple-stranded complex 1A.2U regardless of the component ratio in solution[98].

Some data on the stoichiometry of oligomer–polymer complexes formed with participation of the oligonucleotides of adenylic, deoxyadenylic, and thymidylic acids are presented in Table 4.

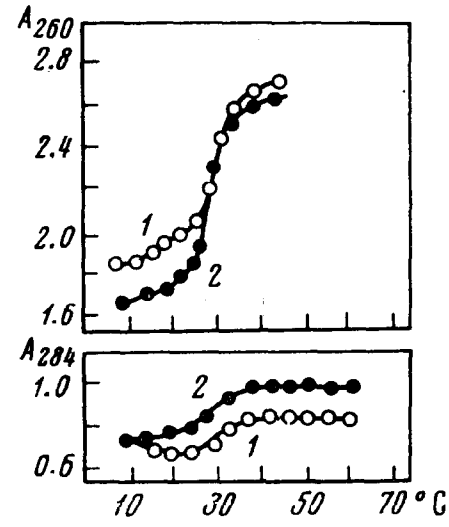


Figure 4. The melting of the structures formed by $d(pA)_8$ with poly dT for different component ratios in solution: 1) 1A–1T; 2) 1A–2T (0.15 M NaCl, pH 7.0).[28]

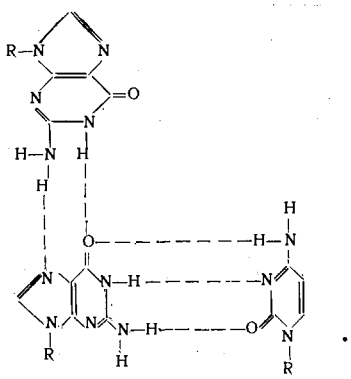
Table 4. Effect of various factors on the stoichiometry of A–U(T) complexes.

System	Component ratio in solution	Complex formation on conditions	Stoichiometry of complex	Refs.
$(pA)_m$—poly U	1A-2U	1*M* NaCl, 0.001*M* $MgCl_2$, 0.002*M* phosph. buffer, pH 7.4	1A-2U	35
$m \geqslant 3$	1A-1U	ditto	1A-2U	35
	1A-2U	0.001*M* MgCl, phosph. buffer, pH 7.2	1A-2U	35
	1A-2U	0.1*M* NaCl, 0.01*M* $MgCl_2$, 0.05*M* cacodylate buffer, pH 7.0	1A-2U	99
	1A-1U	0.1*M* NaCl, 0.002*M* phosph. buffer, pH 7.4	1A-2U	35
$A(pA)_m$—poly U				
$m \geqslant 2$	1A-2U	0.5*M* NaCl, 0.04*M* phosph. buffer, pH 7.3	1A-2U	81
	1A-1U	0.1*M* NaCl, 0.002*M* phosph. buffer, pH 7.4	1A-1U	35
$m=1$	1A-1U	0.001*M* $MgCl_2$, 1*M* NaCl, 0.002*M* phosph. buffer, pH 7.4	1A-1U	35
$d(pA)_m$—poly dT	1A-2T	0.04*M* phosph. buffer, pH 7.0	1A-2T	28
$m \leqslant 12$	1A-1T	ditto	1A-2T	28
$m > 12$	1A-1T	»	1A-1T	28
$m = 4 - 25$	1A-1T	0.008*M* $MgCl_2$, 0.04*M* phosph. buffer, pH 7.0	1A-2T	28
$m \leqslant 16$	1A-1T	0.15*M* NaCl, 0.015*M* citrate buffer, pH 7.0	1A-2T	28
$m > 16$	1A-1T	ditto	1A-1T	28
$d(pT)_m$—poly dA	1A-1T	0.04*M* phosph. buffer, pH 7.0	1A-1T	28
	1A-2T	0.008*M* $MgCl_2$, 0.04*M* phosph. buffer, pH 7.0	1A-1T	28
$d(pT)_m$—poly A	1A-2T	1.0*M* LiCl, 0.01*M* cacodylate buffer, pH 6.8	1A-2T	28

Stoichiometry of G–C complexes. The study of the formation of complexes involving G–C pairs is made extremely difficult by the tendency of guanylyl derivatives to undergo self-association. Numerous studies[99–102] have shown that, under conditions favourable for complex

formation (low temperature, high ionic strength), polyguanylic acid exists in the form of stable aggregates. For this reason, it has not so far been possible to obtain complexes of poly G with cytidylyl oligonucleotides. With decrease of the degree of polymerisation, the tendency towards self-aggregation falls appreciably (but does not disappear altogether), which makes it possible to detect the G–C interaction in the systems oligo G.poly C.

The first data on the stoichiometry of such complexes were obtained by Lipsett[60,74], who investigated the formation of complexes by short guanylic acid oligomers (GpG, GpGp, and GpGpGp) with poly C. On the basis of mixing curves, she concluded that, depending on the temperature and the incubation time, these oligonucleotides can form two types of complexes in a neutral medium: 1G1C (see p. 56) and 2G.1C, in which the guanine bases are linked:



The author believes that the two-stage melting of the complex confirms this structure (Fig. 5).

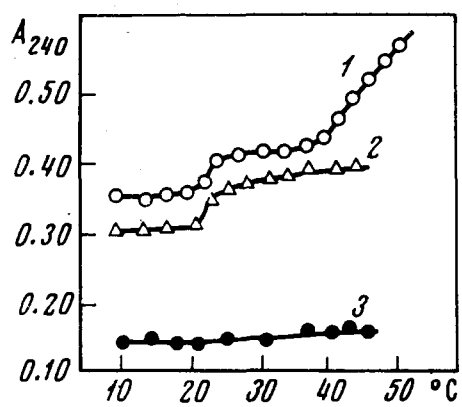


Figure 5. Melting curves: 1) for the complex GpGpGp. .poly C (2G.1C); 2) of the self-association complex GpGpGp; 3) of poly C (0.2 M NaCl, pH 6.2).[74]

However, the mixing curves, which do not have a distinct extremum, show that complex formation in the system is complicated by other, secondary processes, possibly the formation of the self-aggregate GpGpGp. One cannot rule out the possibility that the first stage in the melting profile (Fig. 5) is due to the melting of the self-aggregate GpGpGp, while the second reflects the decomposition of the double-stranded complex 1G.1C.

In the region pH < 6 the oligo G-poly C mixing curve has a distinct minimum at a cytidine mole fraction of 0.66, which indicates the presence of a triple-stranded complex 1G.2C.[74] The formation of a structure of this type was discussed earlier in connection with complexes of guanosine monomers with poly C and is associated with the protonation of polycytidylic acid. Possible schemes for the binding of the bases in the 1G.2C structure were presented above (p. 61).

Thus the results concerning the stoichiometry of oligomer–polymer complexes lead to the following conclusions. Complementary oligo- and poly-nucleotides with a monotonic sequence can form in aqueous solutions double- and triple-stranded helices. The stabilities of the complexes are not the same and are determined in many respects by the structure of the oligomer (the nature of the heterocyclic bases, chain length, etc.). However, with an appropriate choice of conditions (component ratio, pH, ionic strength), it is possible to obtain complexes having the required stoichiometry. In this connection we may recall that the formation of triple-stranded structures is promoted by the presence of purine groups in the oligomer, the presence of ribose residues in the polynucleotide chain, a high ionic strength, and the presence of Mg^{2+} ions. The formation of double-stranded complexes is as a rule observed at a low concentration of salts in the absence of bivalent metal ions. The pH of the solution plays an important role in the stoichiometry of the complex formed in the G–C interaction.

The stability of oligonucleotide–polynucleotide complexes. Thermodynamic parameters of the systems. Triple-stranded polynucleotide complexes can give rise to single-stage or two-stage melting depending on the ionic strength of the solution[90]. The effect of the concentration of the salts on the fusion curves for oligomer–polymer complexes was not specially studied. However, in most of the oligonucleotide–polynucleotide systems the thermal melting profiles are single-stage regardless of ionic strength[35,81,98]. This implies that triple-stranded complexes of oligomers with polymers dissociate, like double-stranded complexes, directly to the initial components without passing through a double-stranded intermediate.

The presence of G–C pairs stabilises the native DNA helices[103]. This is also characteristic of oligomer–polymer systems and is reflected by an increase in the melting points of the complexes containing the G–C pairs. Thus the melting point of the complex of GpG with poly C is 26°C, while that of the complex of ApA with poly U is only 6°C under analogous conditions[35,60].

The thermal stability of the complexes depends on which type of oligomer (purine or pyrimidine) is involved in complex formation. It has been observed that the complexes oligo Pu–poly Py are more stable than oligo Py–poly Pu. For example, the melting point of the complex $(pA)_8$.poly U is 52.8°C, while that of the complex $(pU)_8$. .poly A is 20°C.[104] The reason for the difference between the thermal stabilities of such structures is probably the greater strength in the case of the purine derivatives of the interplanar interactions stabilising the oligomers–polymer helices.

Lipsett et al.[35] showed that, under optimal complex formation conditions, the percentage of hypochromicity in the oligo A-poly U system is 35 for all oligomers, starting

with the trinucleotide, i.e. corresponds to the hypochromic effect of the formation of a triple-stranded helix poly A. .2poly U. Consequently the chain formed by adenylyl oligomers in the complex can be regarded as a continuous pseudopolymeric chain, in which the individual units (oligomers) are linked by vertical interactions.

The situation is different for pyrimidine oligonucleotides. The hypochromic effect observed in the formation of a complex of oligo dT with poly A is smaller than the hypochromic effect for the corresponding polymer–polymer complex. Rich and Tinoco[105] suggested that thymidylic acid oligomers interacting with a polynucleotide are not linked to one another and form independent short helices.

The values of the hypochromic effect for the complexes formed by oligo dT with poly A were calculated for oligomers of different lengths with the aid of the quantitative theory of the hypochromic effect developed by Rich and Tinoco[106].

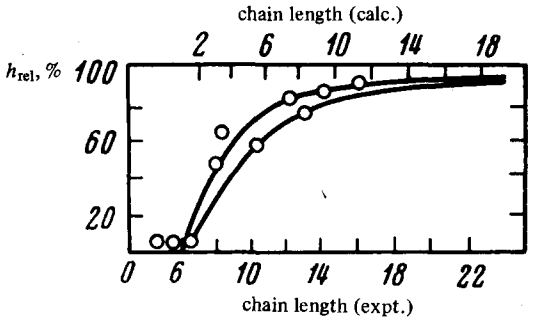


Figure 6. Variation of the hypochromic effect of the complex oligo dT.poly A as a function of the oligomer chain length at 262.5 nm ($h$rel, % is the percentage of hypochromicity calculated in relation to the hypochromicity of the complex poly A.poly U at pH 6.9).[105]

Fig. 6 shows calculated plots (continuous curve) of the relative hypochromic effect as a function of the length of the oligomer chain, the circles representing the experimental hypochromic effects. The experimental hypochromic effect for the heptamer corresponds to the theoretical value calculated for the dimer. This difference does not change with increase in the oligomer chain length up to the eicosanucleotide and makes it necessary to conclude that for any oligo dT 4–6 bases (probably 2–3 at each end) are not included in the stacking interaction, which probably results in a less ideal and stable structure than for the complex oligo A.2poly U.

With increase in the oligomer chain length, the stability of oligonucleotide–polynucleotide complexes rises[60,74,88,103]. A linear relation between the melting point and lg m (or $1/m$), where m is the oligomer chain length, has been established both theoretically[28] and experimentally[85]. The relation shows that the melting points of complexes of short oligomers differ very appreciably from one another, but for longer oligomers the differences between the melting points of the complexes become insignificant. The observed relation is consistent with the statistical-mechanical treatment of cooperative oligomer–polymer interactions described by Magee et al.[67] and Damle[70]. Michelson and Monny[89,104] studied the thermal stabilities of complexes as a function of the oligomer chain length (m) and established that, for a given series of oligomers, the plots of the reciprocals of the melting points against lg m are parallel, i.e. their slope is independent of the nature of the polynucleotide involved in the formation of the complex. It is determined by the structure of the oligomer (the nature of the heterocyclic bases, the presence of terminal phosphate groups, the type of internucleotide bond, etc.). There is a possibility of a break in the $1/T$m–lg m relation, indicating a change in the stoichiometry of the interaction. Indeed, since double- and triple-stranded complexes have different thermal stabilities, the slopes of the plots for these complexes should be different.

The system oligo I–poly C is convenient for the investigation of oligomer–polymer interactions[107]. The stoichiometry of the resulting complexes is always 1I.1C and their optical properties are similar to those of the poly I. .poly C systems[8,59]. However, the stability of the oligo I. .poly C complexes is much lower than that of oligo A.2poly U. Thus the complex ApA.2poly U is not difficult to obtain, while the complex IpI.poly C could not be detected and the minimum length of the inosine oligomers forming complexes with poly C was 5–6 monomeric units depending on the conditions[104].

The variation of the stability of the oligomer–polymer complexes with oligomer concentration, which decreases with increase in the oligomer chain length, has been determined. Thus the melting point of the complex $A(pA)_6$.2poly U decreases by 13 deg on 1000-fold dilution of the solution, while the melting point of the complex $A(pA)_4$.2poly U, containing a shorter oligoadenylate, decreases by 14 deg on 100-fold dilution[29]. Blake[33] confirmed this behaviour in a study of the stability of the complexes $(Ap)_4$.2poly U as a function of the tetramer concentration. Cassani and Bollum[28] noted an appreciable influence of the oligomer concentration on the width of the thermal transition ΔTm.

It was noted in a number of cases that the stability of the oligomer–polymer complexes depends on the nature of the sugar ring. The complexes of the ribo-series apparently have a higher thermal stability than those of the deoxyribo-series, which is largely consistent with the characteristics of the polymer–polymer interaction[95,108]. Knorre and coworkers[109] showed that, when the sugar residue of the terminal nucleoside in the oligomeric component is modified, the capacity of the latter for complex formation persists. Thus 2′,3′-*O*-benzylidene derivatives of oligoadenylates give rise to complexes whose properties are identical to those of the complexes of unmodified oligomers, the benzylidene group being displaced from the helix.

The available data about the influence of the terminal phosphate group on the stability of the complex are fairly contradictory. Uhlenbeck et al.[30], who investigated the thermal stabilities of the complexes formed by (Ap)mA and $(Ap)_{m+1}$ with poly U, noted the destabilising effect of the 3′-phosphomonoester group. Thus the introduction of a terminal 3′-phosphate into the tetramers and pentamers reduces the melting points of the complexes of these oligomers with poly U by 8 deg, which the authors believe can be explained by the increased electrostatic repulsion between the oligomers and the polymer chains in the presence of a terminal phosphomonoester group. A similar effect, decreasing appreciably with increase in chain length, has been observed for the system oligo G–poly C.[74]

However, according to Lipsett's data[35], only the terminal 5'-phosphate group has a destabilising effect, while the 3'-phosphomonoester group increases the thermal stability of the complex (Table 5). The author does not explain this fact satisfactorily. Presumably the presence of the phosphomonoester groups should destabilise the complex regardless of their positions in the oligomer chain and the degree of destabilisation can be different for the 3'- and 5'-phosphates, since these groups are known to have different effects on the secondary structures of the oligonucleotides themselves[110].

Table 5. Effect of the terminal phosphate group on the melting points of the complexes oligo A.2poly U (0.18×10^{-3} M nucleotide, 1 M NaCl, 0.001 M $MgCl_2$, pH 7.4).[35]

Position of terminal phosphate	Oligomer chain length			
	2	2	4	5
5'-Phosphomonoester group	7	17	29.5	37
3'-Phosphomonoester group	5	23	33.2	40.5
Without phosphomonoester group	6.2	17.4	31.3	

The formation of complexes by poly U with 5'-oligodeoxyadenylate amides, differing in the structure of the amide fragment and the length of the nucleotide chain, has been investigated by ultraviolet spectroscopy[111]. It was observed that the amide group does not alter the symmetry of the complex (1A.2U), but reduces somewhat its melting point. The destabilising influence of the amide group depends on its structure and decreases with increase in the oligomer chain length.

The nature of the internucleotide linkages in the oligomer molecule has a definite influence on the thermal stabilities of the complexes. It has been noted that the fusion of complexes of isomeric oligonucleotides with the 2'-5'-phosphodiester linkage in the systems oligo A–poly U and oligo G–poly C gives rise to a transition of the same width as complexes of the oligomers with the natural internucleotide linkage, but their melting points are somewhat lower[35,74].

The influence of the defects in the nucleotide sequence of the complementary oligomer on the stability of the oligonucleotide–polynucleotide complexes is of great interest. It has not been established unambiguously whether the non-complementary bases are incorporated into the helix or whether they form loops with breakdown of the stacking interaction between adjacent heterocyclic bases. A study of polynucleotide complexes revealed that the steric disposition of the non-complementary bases in the helix depends on their nature and number[30,112–115].

When the content of the non-complementary base is above a critical value, which depends on the type of system, a complex is not formed[114,115]. Only the frequency and length of the non-complementary sections of the chain are important[59], while the requirements which must be met by their positions in the chain as well as the steric requirements for the formation of complementary pairs at the ends of the helical section are less rigorous than within the section[82].

Uhlenbeck et al.[30] investigated the influence of terminal non-complementary bases in the oligomer on complex formation in the systems X(pA)m–poly U and (Ap)mX–poly U (X = C, U, or G) and reached the following conclusions.

1. The presence of a non-complementary base at one of the ends of the oligonucleotide lowers the stability of the complex.

2. The non-complementary base is displaced from the helix and the polymer is filled without gaps, for example in the interaction between poly U and the oligomers $C(Ap)_4$ and $(Ap)_4C$ the minimum on the mixing curve should occur at a uridine mole fraction of 0.667 if all the oligomer bases interact with the uracil residues, while the experimental curve has a minimum at a uridine mole fraction of 0.612. This means that the cytosine residues do not occupy any sites on the matrix.

3. The introduction of a cytosine residue in the middle of the oligomer has a weaker distabilising effect. The authors believe that this is largely due to the greater degree of solvation of the non-complementary cytosine ring, which has a higher dipole moment than the guanine and uracil rings.

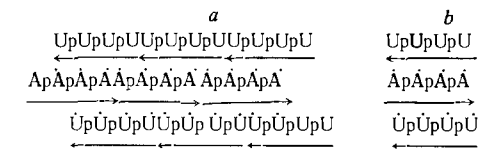
4. A non-complementary base at the 3'-end of the oligomer molecule destabilises the complex to a greater extent than the same base at the 5'-end.

V. INTERACTION OF COMPLEMENTARY OLIGONUCLEOTIDES

The study of complexes of complementary oligonucleotides is particularly important, since it yields information about the stability of short helices, which appear to be important structural elements in ribonucleic acids[53]. However, heterogeneous oligomers with a complex nucleotide sequence are so far almost inaccessible to study owing to the difficulty of their synthesis. Oligomeric complexes formed by oligonucleotides with a monotonic sequence have been most thoroughly studied. The kinetics of complex formation involving flow and relaxation (temperature jump) methods have been studied recently in systems of this kind[36,57,116–118].

Complexes of oligonucleotides with a monotonic nucleotide sequence are apparently not truly oligomeric. These are the so called "concatomers" having a structure similar to that of polymer–polymer complexes and differing from the latter only by the presence of breaks in the chains of the helix.

For example, the triple-stranded complex 1A.2U, formed by the tetranucleotides ApApApA and UpUpUpU, can be represented by the following concatomeric scheme (a):



The formation of such structures rather than dimeric or trimeric complexes is confirmed by the higher molecular weight of the complexes, greatly exceeding three times the molecular weight of the oligomer[48,81]. The formation of concatomeric structures in those cases where it is possible is probably thermodynamically more favourable than the formation of individual short helices of type *b*.

The stoichiometry of concatomeric complexes has been inadequately studied. It has been shown for the interaction of short oligo A oligomers with oligo U by CD, infrared, and ultraviolet spectroscopic methods[53,81] that the stoichiometric formula of these complexes is 1A.2U regardless of the component ratio and the ionic strength of the solution.

Pörschke[23] determined the critical oligomer chain length ($n = 7$) above which the formation of double complexes is possible. The author believes that for shorter oligomers ($n \leq 7$) both double and triple helices are formed.

On the basis of the ultraviolet spectrum of the complex oligo A.oligo dT, Hoggett and Maass[36] suggest the stoichiometric formula 1A.1T. Complexes of oligo G with oligo C have not so far been studied.

The thermal stabilities of the concatomeric complexes formed by adenylic acid oligomers with oligo U or oligo dT have been studied in fair detail[5,36,81]. The stability of such complexes greatly depends on the length of the oligomers and their concentration in solution. Thus the complex $A(pA)_3.3U(pU)_3$ (nucleotide concentration 0.12 M; 0.04 M $MgCl_2$; pH 7.0) melts at 17°C, while $A(pA)_5.2U(pU)_5$ has a melting point of 27°C under these conditions[53]. The shorter the oligomers the higher should be their concentration for complex formation to be appreciable. Thus the complex formation reaction between $A(pA)_7$ and $d(pT)_8$ takes place even at a nucleotide concentration of 8.5×10^{-6}, while the trinucleoside diphosphates ApApA and UpUpU interact only at a concentration of 0.12 M.[53]

The problem of the minimum oligomer size necessary for complex formation has been discussed in the literature for a long time[5,48,103]. Studies by Brahms et al.[119] showed that, at an overall nucleotide concentration of 10^{-4} M, the smallest oligomers are the heptamers. Felsenfeld and Miles[53], who increased the nucleotide concentration by a factor of 1000, demonstrated the existence of complexes of tri- and tetra-mers. The interaction between the complementary mono- and di-nucleotides in aqueous solutions has not so far been observed, although it does apparently occur in organic solvents (chloroform, dimethyl sulphoxide)[120,121].

Complex formation depends on the nature of the oligomers. Thus the formation of a complex in the system oligo dT–oligo dA at a nucleotide concentration of 0.001 M is observed starting with the pentamer of thymidylic acid and the tetramer of adenylic acid[5]. Maurizot et al.[122] observed a relation between complex formation and the structure of the sugar. Thus a comparative study by the CD method of the oligomer mixtures dA_n–dT_n and rA_r–rT_n ($n = 3$–8) in 4.7 M KF solutions at −20°C and a nucleotide concentration of 0.001 M established that deoxyribo-oligomers begin to form a complex starting with trimers, while their ribose analogues begin to form complexes starting with hexamers.

The effect of the ionic strength of the solution on complex formation in the majority of oligomer–oligomer systems has been studied as a rule at high ionic strengths (0.5–1.0 M NaCl) and in the presence of $MgCl_2$.[5,36,48,81] It was noted that, when oligo dT reacts with oligo A, the relation between the melting point and $\lg I$ (I is the ionic strength of the solution) deviates somewhat from linearity[36], in agreement with the behaviour of the system poly dT–poly A.

The formation of concatomers[108] is probably favourable also in this case, when the oligomers have an alternating nucleotide sequence. For example, oligo (CA) likewise forms overlapping structures with oligo (TC).[123]

However, when the oligomer has a self-complementary alternating sequence, intermolecular complex formation is not observed. Studies by Scheffler and coworkers[124,125] showed that the structure formed on folding the oligomer chain in two is more favourable for the oligonucleotide $d(TA)_m$. The melting point of the complex then also increases with the oligomer chain length, but is independent of the oligomer concentration.

Complexes of oligonucleotides with a non-monotonic nucleotide sequence were begun to be studied only in the last few years when considerable advances were made in chemical methods for the synthesis of oligomers with a specified sequence[126]. It was established that the interaction of non-monotonic oligonucleotides, uncomplicated by self-aggregation, involves the binding of two (or three) molecules of complementary oligomers with formation of short oligomer–oligomer helices[48,63,127,128]. In this case the general rules are approximately the same as for the formation of concatomeric structures.

The thermal stabilities of a number of complexes of nucleotides with a fairly wide variety of compositions were studied by Khorana and coworkers[127,128], who established that in the presence of Mg^{2+} there is a possibility of complex formation involving relatively short oligonucleotide blocks. Thus complexes of tetranucleotides with deca- and eicosa-nucleotides were obtained at a low temperature (0–5°C).[123] It was noted that, with increase of the content of G–C pairs, the oligomer–oligomer helices are stabilised. A similar behaviour was discovered also in a study by Martin et al.[129]

The attempt to obtain shorter oligomer–oligomer helices was unsuccessful. Jaskunas et al.[47], who investigated by the ORD method a large number of systems consisting of complementary trinucleoside diphosphates, found complexes only for the GpGpG–GpCpC pair (at a nucleotide concentration of 0.01 M in the presence of 0.001 M $MgCl_2$ at pH 7 and 1°C). However, the complex formation process is complicated so much by the self-aggregation of the trimers GpGpC that it is impossible to infer the stoichiometry of the interaction.

If the oligomer chain length is equivalent to 8–10 nucleotides, it is possible to obtain fairly stable complexes also from oligomers without guanylic and cytidylic acids[116]. Martin et al.[129] studied the capacity for complex formation of the self-complementary oligonucleotides $(Ap)_mU(pU)_{n-1}$, in which m and n were varied from 3 to 7. The marked concentration variation of the degree of complex formation for such oligomers suggests the formation of intermolecular complexes and rules out the possibility of intramolecular interactions. It was established that the structure of the complex formed is determined by the ratio A/U in the oligomer chain. A double helix is formed for $m \geq n$ but, when $m < n$, the results of sedimentation analysis and the ultraviolet spectra indicate the formation of larger aggregates, probably containing triple-stranded sections. For identical lengths of the A and U blocks in the oligomer ($m = n$), the melting point of the complex increases appreciably with chain length $N = m + n$ (Table 6).

The enthalpies ΔH_1 quoted in Table 6 refer to the formation of 1 mole of A–U pairs and were calculated from the slopes of the concentration variation of the melting point of the complex. The absolute value of ΔH_1 increases with increase in chain length. This deviation from Applequist's ideal model[68], for which ΔH_1 is independent of the oligomer chain length and the overall heat of reaction is defined by the expression $\Delta H_N = N\Delta h_1$, is not surprising, since it is clear that the contributions to the stabilisation of the helix are by no means the same for all the base pairs. Hoggett and Maass[36] showed that, in the interaction of oligo T with oligo A, the enthalpy of formation of the first base pair $\Delta H\beta S$ is positive although low. The enthalpies of formation of terminal base pairs can also differ significantly from the enthalpies of formation of the base pairs within the oligomer chain.

The stabilities of the oligomer–oligomer complexes having the same length and nucleotide composition but different nucleotide sequences are evidently not the same. Indeed, the oligonucleotides $(Ap)_6C$ and $G(pU)_6$ form a more stable complex (m.p. 25°C) than $C(pA)_6$ and $(Up)_6G$ (m.p. 19°C),[48] which may be due to a difference between the stacking interactions of the bases in the isomeric structures[130]. Differences have also been observed in the stabilities of the series of complexes $A_nCG.CGU_n$ (n = 6 or 8), $AnG_2.C_2U_n$ (n = 4 or 5), and $AnG_3.C_3U_n$ (n = 4 or 5) differing in the positions of the G–C pairs, which the authors attribute to differences in the entropy changes[131].

Table 6. Certain characteristics of the complexes formed by the oligonucleotides $(Ap)_mU(pU)_{n-1}$ (10^{-4} M nucleotide, 1 M NaCl, pH 7.0).[129]

Oligonucleotide	$N=(m+n)$	$-N\Delta H_1$, kcal mole^{-1}	$-\Delta H_1$, kcal mole^{-1}	M.p., °C
$(Ap)_3U(pU)_2$	6	—	—	—13
$(Ap)_4U(pU)_3$	8	51	6.4	12
$(Ap)_5U(pU)_4$	10	72	7.2	23
$(Ap)_6U(pU)_5$	12	85	7.1	32
$(Ap)_6G(pU)_4 \cdot (Ap)_4C(pU)_5$	14	107	7.6	40
	10	—	—	29*
				33**
$(Ap)_4CpG(pU)_4$	10	76	—	42.6

*The melting point of the complex calculated for a nucleotide concentration of 0.5×10^{-4} M.
**ditto for a nucleotide concentration of 2×10^{-4} M.

The introduction of a non-complementary nucleotide into the oligomer molecule hinders the formation of a complex and lowers its stability. Thus a study has been made of the capacity for interaction of the two oligomers $(Ap)_mC(pU)_n$ and $(Ap)_mG(pU)_n$, but in separate solutions and not in a mixture as in the previous study[132]. The cytidine and guanosine monomers disturb the self-complementarity of these oligomers and the destabilisations of the complexes due to them are not the same. The oligomer containing cytidylic acid forms a less stable intermolecular complex than the oligomer with guanylic acid (Fig. 7).

For comparison, the same figure presents the melting profile for the complex formed by $(Ap)_5U(pU)_4$ under analogous conditions. Analysis of the melting points of these complexes for different m and n showed that the introduction of the cytosine residue into the oligomer molecule lowers the stability just as much as the removal of two A–U pairs. The cytidylyl nucleotide probably forms a loop in the structure and displaces from the helix at least a pair of nucleotides adjoining it in the chain. The higher stability of the complex formed by the oligomer $(Ap)_mG(pU)_n$ compared with that of the oligomer $(Ap)_mC(pU)_n$ can be explained on the assumption that the guanylyl residue is not displaced from the helix, like the cytidine residue, but is incorporated in it, forming a G–U pair. The oligomeric molecules should then be displaced relative to one another:

ApApApApGpUpUpUpU
UpUpUpUpGpApApApA .

This structure is confirmed by the fact that its stability is close to that of the complex

ApApApApApUpUpUpU
UpUpUpUpApApApApA .

If 4–6 cytidylyl residues are inserted in the oligomer between homogeneous blocks, the molecule folds in two with formation of a single-stranded cytidylyl loop and a structure simulating the tRNA fragments[133]. Complexes of oligomers, in which not all the bases are paired have also been studied, in particular those formed by deca- and nona-nucleotides or deca- and hepta-nucleotides[127]. It has been noted that the thermal stabilities of these complexes decrease with the increase of the non-complementary backbone. For example, the complex of two eicosanucleotides, forming a helix from ten nucleotide pairs.

GTACCCTGTCAGAGGCCAAC
GCTCCCTTAGCATGGGACAG ,

has no cooperative melting profile at all[128], while the complex of a deca- and nona-nucleotide (GAACCGGAGA and TCTCCGGTT) melts over a fairly narrow temperature range (m.p. 40°C).[227] The destabilisation of the eicosanucleotide complex is due to the absence of an ordered steric structure from the single-stranded section of the helix. The inclusion of the single-stranded section in the complex with another oligomer leads to a sharp increase of the stability of the structure[127, 128].

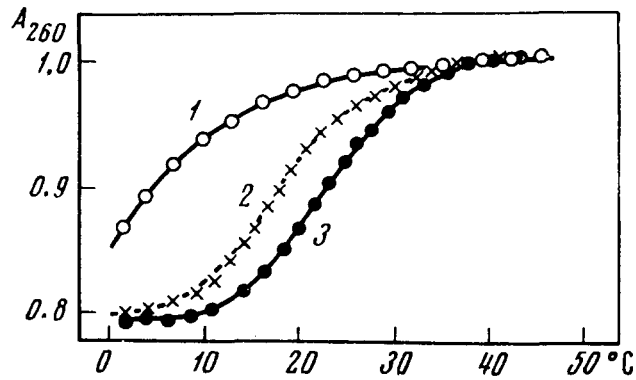


Figure 7. Melting curves for intermolecular oligomer complexes: 1) $(Ap)_5C(pU)_5$; 2) $(Ap)_5G(pU)_5$; 3) $(Ap)_4ApU(pU)_4$ (2.5×10^5 nucleotide, 1 M NaCl).[132]

Analysis of the fundamental relations established in the study of the complementary properties of mono- and oligonucleotides will undoubtedly help in predicting, in a broad outline, the behaviour of systems which have not so far been investigated and in assessing the scope of the complex formation, the stoichiometry of the interaction, etc. However, these characteristics of comparatively simple synthetic systems cannot be applied mechanically to oligomer–oligomer interactions involving native macromolecules with a complex steric structure. Complexes of synthetic oligonucleotides with native polymeric molecules or their fragments, studies on which began recently[134–139], are probably more useful models.

A number of new publications appeared recently. Studies on monomer–polymer [140–143] and oligomer–polymer complexes [144–146] are being continued. Oligomer–oligomer systems which both monotonic [147] and non-monotonic sequences of bases [148–150] are being investigated vigorously.

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The Structural Chemistry of Organic Compounds of Mercury and Its Analogues (Zinc and Cadmium)

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Information on the structure of organometallic compounds of zinc, cadmium, and mercury published up to 1973 is summarised. Detailed consideration is given to true organometallic compounds, containing a metal-carbon bond. Compounds in which a carbon atom (hydrocarbon radical) is separated from the metal atom by a heteroatom are mentioned only for comparison, and no systematic description of their structures is given. The Review covers results obtained by X-ray and neutron diffraction, gas-phase, electron diffraction, and in part microwave and Raman spectroscopy. A list of 90 references is included.

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I. INTRODUCTION

Structural examination of compounds of zinc, cadmium, and mercury—members of subgroup II*b* of Mendeleev's Periodic System and having outer electron shells of similar structure—reveals significant differences in their stereochemistry: whereas a tetrahedral bond configuration is more characteristic of zinc and cadmium, mercury prefers a linear configuration with two short bonds, and this geometry of mercury compounds is little distorted by additional coordination interactions. Orgel[1,2] explained the structure of this type of mercury compound with strongly electronegative ligands in terms of their conferring a high positive charge (formally +2) on its atom: transition from the $5d^{10}$ (Hg^{2+}) electronic configuration to $5d^{9}6s^{1}$ followed by d_z2s hybridisation requires relatively little energy (5.3 eV), considerably less than for zinc and cadmium. Such hybridisation presupposes the existence either of two stable bonds in the *z* direction and four weak bonds in the *xy* plane or four stable bonds in the *xy* plane and two weak bonds in the *z* direction. The former alternative is preferred, although this cannot be explained in terms of Orgel's concepts.

In compounds with less electronegative substituents, in which the mercury atom has a small positive charge (formally +1) and the $5d^{10}6s^{1}$ configuration, the energy necessary for the transition $5d^{10}6s^{1} \rightarrow 5d^{10}6p^{1}$ is really not so small (~ 6 eV).[2,3] Linear *sp* hybridisation is therefore most favourable, with the use of only one higher *p*-level. In zinc and cadmium the energy difference between *s* and *p* levels is smaller, which facilitates sp^3 hybridisation.

Since the structure of organomercury compounds differs from that of organozinc and organocadmium compounds, they are discussed in different Sections. The stereochemistry of organomercury compounds is dealt with in Section II, where ideas put forward by Grdenić[2] are used. Subsections II, 1 and II, 2 examine the structures of aliphatic and aromatic organomercury compounds respectively. The presence of intramolecular coordination is discussed in subsection II, 3, and finally crystal structures with intermolecular coordination of the mercury atom are described in II, 4. However, assignment to a particular subsection is often difficult, both owing to the impossibility of establishing coordination on the basis of available data and because the original paper lacks the appropriate information (in particular no analysis of intermolecular distances is given, and sometimes even the atomic coordinates are missing). Structures of organomercury compounds determined by X-ray diffraction are usually not very accurate, owing to the great difference in atomic number between mercury and the other atoms present in the molecule. Section III deals with the structures of organozinc and organocadmium compounds, which have been little studied.

II. ORGANOMERCURY COMPOUNDS

1. Aliphatic Derivatives

The first information on the structure of dimethylmercury was obtained during 1936-1937, when gas-phase electron diffraction gave values of 2.20 and 2.23 Å[4,5] for the mercury-carbon bond length in this molecule. However, 2.094(5) Å has since been obtained[6] from the Raman spectra. This value has recently been confirmed by a second electron diffraction investigation: the internuclear distance in the linear CH_3-Hg-CH_3 molecule is 2.083 Å.[7]

Compound	Hg-C, A	Hg-X, A	Ref.
CH_3HgCH_3	2.083 (5); 2.094 (5)	—	6,7
CH_3HgCl	2.061 (20)	2.282 (5)	8
CH_3HgBr	2.074 (15)	2.406 (5)	8
CH_3HgI	2.087 (10)	2.528 (5)	9

Closely similar values have been obtained by microwave spectroscopy for the methylmercury halides (Table). It is evident that the presence of a halogen atom in the molecule shortens the mercury-carbon bond, an effect which diminishes in the sequence Cl > Br > I, so that the bond length in methylmercury iodide is the same as in dimethylmercury.

X-Ray examination of several alkylmercury halides—methylmercury, ethylmercury, propylmercury, and butylmercury chlorides and ethylmercury bromide—by means of projections[10] gave values of 2.06(3), 2.50, and 2.51 Å for the bonds between mercury and carbon, chlorine, and bromine respectively. The mercury–halogen bond lengths differ significantly from the above values, probably because of the lower accuracy of X-ray examination. This method gave 2.43 Å for the mercury–bromine bond length in *trans*-2-chlorovinyl mercury bromide ClCH:CH.HgBr.[11]

From the bond lengths in the above compounds and in those of type HgX_2 investigated by electron diffraction in the vapour phase, with the Schomaker–Stevenson correction for the electronegativity difference, Grdenić proposed[2] the value 1.30 Å for the covalent radius of mercury with a linear bond configuration. This value corresponds satisfactorily to the additivity rule for free molecules of the types HgX_2 and $HgXX'$. This rule is not always satisfied in crystalline structures, owing to the influence of surrounding molecules.

sp-Hybridisation of the mercury atom presupposes that these dihalide molecules have a linear structure, but it is interesting to trace to what extent linearity is preserved in organomercury compounds. From the vibrational spectra of methylmercury cyanide CH_3HgCN it was concluded[12] that linearity of the C–Hg–C(N) fragment was disturbed in this compound. Examination of crystals by X-ray and neutron diffraction[13,14] showed in both cases that the angle at the mercury atom was 180 ± 2°. The Hg–CH_3 and Hg–CN bond lengths were 2.15(5) and 2.01(5) Å according to the X-ray results, and 2.08(2) and 2.05(1) Å respectively according to neutron diffraction. It is interesting that the latter method distinguished between the nitrogen and carbon atoms, and showed that mercury was attached to the carbon atom of the cyano-group.

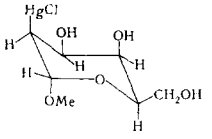
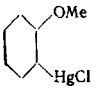


Figure 1.

X-Ray examination of DL-penicillaminatomethylmercury[15] indicated that the methylmercury group is attached to the amino-acid through a deprotonated mercapto-group $CH_3.Hg.S.C(CH_3)_2.CH(NH_3^+).COO^-,H_2O$. The CH_3–Hg–S fragment is nearly linear (176(2)° and 179(1)° in two independent molecules). The mean Hg–C and Hg–S bond lengths are 1.90(6) and 2.38(1) Å, and the angle at the sulphur atom is 109°.

A linear configuration has been found for mercury also in methoxycarbonylmercury chloride Cl–Hg–$COOCH_3$ (X-ray examination by projections).[16] The Hg–C and Hg–Cl bond lengths of 1.96 and 2.35 Å differ from those found in methylmercury chloride[8] and in mercury(II) chloride[2], but the poor accuracy makes the reality of these differences dubious.

X-Ray investigation[17] of two diastereomers—(I) $\alpha(dd,ll)$ and (II) $\beta(dl,ld)$—of 2-methoxycyclohexylmercury chloride



showed that in (I) the Hg–C and Hg–Cl bond lengths were 2.34 and 2.53 Å, with the ClHgC angle 178°; the corresponding values in (II) were 2.15, 2.50, and 180°. The molecules differ in the relative orientation of the substituents about the cyclohexane ring. Thus the intramolecular Hg...O distances in (I) and (II) are 4.06 and 3.06 Å.

Structure determination by means of X-rays showed[18] that the Hg–Cl bond length in methyl 2-chloromercury-2-deoxy-α-D-talopyranoside (Fig. 1) is 2.38(10) Å. Preliminary examination of dibenzylmercury crystals[19] established only the partial position of the mercury atom in the cell (space group $P4_2/n$, $z = 4$).

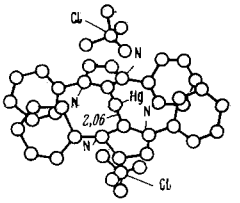


Figure 2.

The mercury–carbene complex $[Hg(C_{15}H_{12}N_2)_2](ClO_4)_2$ possesses an interesting structure (Fig. 2).[20] The cation is located at the centre of symmetry, so that the configuration of the mercury bonds is strictly linear. The Hg–C bond length of 2.06(1) Å coincides within the limits of accuracy with the sum of the covalent radii of mercury and sp^2 carbon (1.30 + 0.74 Å).

2. Aromatic Compounds

Measurements of the dipole moments of diarylmercury compounds indicate significant polarity[2,21,22], which might be explained by non-linearity of the C–Hg–C fragment. It was therefore of interest to undertake structure determinations on these compounds.

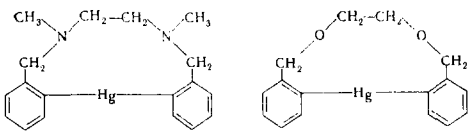
Two methods—X-ray structure determination[23–25] and gas-phase electron diffraction[26]—have been used to examine diphenylmercury. This planar molecule is situated at a centre of symmetry in the crystal, so that the C–Hg–C fragment is strictly linear. The structure was refined on the assumption that the Hg–C bond length was 2.10 Å: i.e. this parameter was not objectively determined. Electron diffraction in the gas phase led to the fairly accurate value of 2.092(5) Å for the Hg–C internuclear distance. The CHgC angle was not determined experimentally, but was assumed to be 180°.

Comparison of the mercury–carbon bond length thus obtained with that found in aliphatic organomercury compounds reveals no contraction on passing from sp^3 to sp^2 hybridisation of the carbon. On the other hand, it was of interest to ascertain the extent to which the state of

hybridisation of the carbon atom attached to mercury in organomercury halides affects the mercury–halogen bond length. Examination of phenylmercury bromide vapour by electron diffraction[27] showed, on the assumption that the C–Hg–Br fragment was linear, that the Hg–Br bond length was 2.435(4) Å, rather longer than the 2.40 Å in methylmercury bromide (see above): i.e. it was established that the organic substituent attached to the mercury atom influences the length of the mercury–halogen bond.

X-Ray structure determination on di-*p*-tolylmercury established that the mercury–carbon bonds were collinear[28,29] (the planar molecule was located at a centre of symmetry). The Hg–C bond length of 2.08 Å coincides within the limits of accuracy with the sum of the covalent radii. The great scatter in the carbon–carbon bond lengths and angles in the phenyl rings (1.39–1.44 Å and 116–124°) is an indication of the difficulty of locating light atoms in the structures of organomercury compounds.

In most of the symmetrical mercury compounds examined by X-ray diffraction the mercury atom is situated at a centre of symmetry, so that the C–Hg–C fragment has a strictly linear structure in the crystal. In bispentafluorophenylmercury $(C_6F_5)_2Hg$, in whose crystal structure the molecule is located at a common position [sic: the molecular crystal has four molecules in the unit cell (Ed. of Translation)], the CHgC angle is 176.2(1.2)°.[30] This value probably represents the limits within which linearity of X–Hg–X bonds can be disturbed by the packing of molecules in the crystal. It is noteworthy, however, that the distances between mercury and the *ortho*-fluorine atoms—3.32, 3.25, 3.22, and 3.14 Å—are fairly short. The possibility of specific Hg...F interaction is therefore not excluded; this would be analogous to (but weaker than) the coordination interaction of the mercury atom with the *ortho*(2,2′ and 6,6′)-chlorine atoms in bispentachlorophenylmercury[31] indicated by the nuclear quadrupole resonance spectrum. Such interaction may disrupt the linearity. In contrast to diphenyl- and di-*p*-tolyl-mercury, moreover, the $Hg(C_6F_5)_2$ molecule is non-planar in the crystal, with an angle of 59.4° between the planes of the benzene rings.



(I) $HgC_{18}H_{22}N_2$ (II) $HgC_{16}H_{16}O_2$

Figure 3.

The angle at the mercury atom also differs from 180° in the crystal structures of *NN*′-dimethylethylenediamine-ωω′-di-*o*-tolylmercury (I) and ethylenedioxy-ωω′-di-*o*-tolylmercury (II) (Fig. 3),[32] being respectively 172.3(9)° and 173.6(2.1)°. The Hg...O distances of 3.01(4) and 3.19(3) Å in (II) and the Hg...N distances of 2.92(2) and 2.97(2) Å in (I) were regarded as excluding coordination between the atoms, which might have led to some disturbance of bond linearity. Thus these disturbances are probably due to steric stresses.

X-Ray examination of 1-naphthylmercury iodide[33] revealed only the heavy atoms—mercury and iodine—separated by the bond length 2.61 Å.

Thus these subsections 1 and 2 show that a linear bond configuration is most common in organomercury compounds, with the mercury–carbon bond length generally within the range 2.06–2.10 Å.[34] Other bond configurations are rare and atypical in organomercury compounds.

3. Compounds with Intramolecular Coordination of Mercury with a Heteroatom

Coordination between the mercury atom and a heteroatom in the same molecule has recently been increasingly used to explain several anomalies in the physical properties of organomercury compounds, as well as to interpret many of their reactions[27]. In particular, special features of the infrared, nuclear magnetic resonance, and nuclear quadrupole resonance spectra and the dipole moments, as also anomalous effects of *ortho*-substituents, are explained by such coordination interaction[35–37].

X-Ray structure determination and electron diffraction are often used to ascertain the possible presence of intramolecular coordination interaction. The sole geometrical criterion of such interaction is the shortening of the distance between the atoms in comparison with the sum of their van der Waals radii. The presence of interaction can be deduced unambiguously from this criterion only if the contraction exceeds those which may arise from packing effects (~ 0.2 Å). Grdenić[2] suggested 1.50 Å, half the shortest interatomic distance in metallic mercury, as the van der Waals radius; and to allow for several specific coordination interactions he proposed the value 1.73 Å (half the next larger interatomic distance in metallic mercury). These recommendations were based on the intermolecular mercury–halogen distances in the structures of organomercury halides[10]. Since the minimum van der Waals radius proposed by Grdenić exceeds the covalent radius of mercury by only 0.2 Å, it is difficult in several cases to reach, on the basis of the above geometrical criterion, an unambiguous conclusion on the presence of weak coordination interaction. Additional criteria must therefore be adduced in order to establish such interaction.

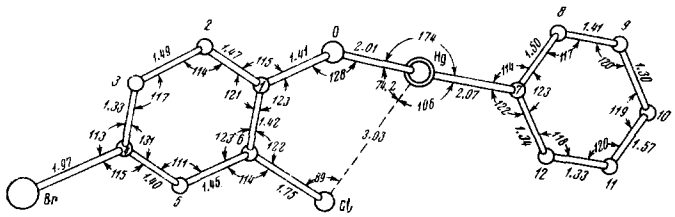
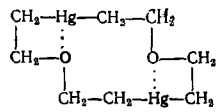


Figure 4.

X-Ray examination of phenylmercury 4-bromo-2-chlorophenoxide (Fig. 4) was undertaken[38] to establish the possibility of intramolecular interaction of the *ortho*-chlorine with the mercury. Such interaction is possible on appropriate rotation of the phenyl ring about the C–O single bond. The angle between the HgOC ω plane and the plane

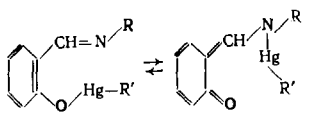
of the benzene ring $C_{(1)}...C_{(6)}$ is found experimentally to be 17°, when the molecule acquires a cisoid conformation, in which mercury and chlorine atoms approach to 3.03(2) Å. This distance is 0.3 Å shorter than the sum of the van der Waals radii of chlorine (1.8 Å) and mercury if the minimum 1.5 Å is adopted for the latter, and 0.5 Å shorter if 1.73 Å is used. It should be noted also that the OHgC angle away from the chlorine atom has diminished to 174(1)°, while the location of the chlorine atom relative to the C–Hg–O fragment is roughly symmetrical (to the extent that this is permitted by the geometrical rigidity of the "metal ring" HgOCCCl): the ClHgO and ClHgC angles are respectively 74° and 106°. All this is evidence of the presence of intramolecular Hg...Cl coordination. The Hg–C and Hg–O bond lengths are respectively 2.07 and 2.01 Å. Thus such interaction does not cause elongation of valency bonds and produces no significant change in hybridisation.

X-Ray structure determination on "diethylenemercury oxide" established [39] that the molecule was dimeric



with strong Hg...O coordination interaction at 2.21(10) Å (sum of covalent radii 1.96 Å) in a twelve-membered ring arranged about a twofold axis. It is strange, however, that such strong interaction barely disturbs the hybridisation of the mercury atom (CHgC angle 176°), which probably indicates the poor accuracy of the work (the structure was determined from projections). The length of the Hg–C bonds in this molecule is 2.14 Å.

An intensive study of metallotropic rearrangements, including metallotropic tautomerism, has begun recently. In particular, electron spectroscopy has provided evidence that phenyl- and methyl-mercury derivatives of *o*-iminomethylphenols are present in solution as equilibrium mixtures of metallotropic benzenoid and quinonoid tautomers, whose proportions vary with the temperature and the polarity of the solvent [40]:



(I) (II)

Transfer of the phenylmercury residue from one reaction centre to the other is facilitated by intramolecular coordination, which is possible if the molecule has a *cis*-conformation relative to the exocyclic carbon–carbon bond. X-Ray structure determination has shown [41] that phenylmercury *o*-methyliminomethylphenoxide is an *N*-derivative of *o*-methyliminomethylphenol with the *cis*-conformation. The triclinic cell contains two independent molecules, having the same geometry within the limits of accuracy. The structure of one of them is shown in Fig. 5. The mean Hg–N and Hg–C bond lengths are 2.12(3) and 1.98(4) Å.

The oxygen atom is distant 2.44 Å from the mercury atom, about 0.4 Å further than the length of the mercury–oxygen covalent bond and 0.4–0.6 Å closer than the sum of the van der Waals radii. In this case there is no doubt about the presence of coordination interaction. Here, as in the preceding structure, the bond angle opposite to the "additional" oxygen atom is diminished to 167°, the greater decrease being consistent with stronger intramolecular interaction between mercury and the heteroatom.

The presence of strong Hg...O coordination interaction implies that the quinonoid structure (II), whose predominance follows from the fact that mercury is covalently bound to the nitrogen atom, is accompanied by the benzenoid form (I).

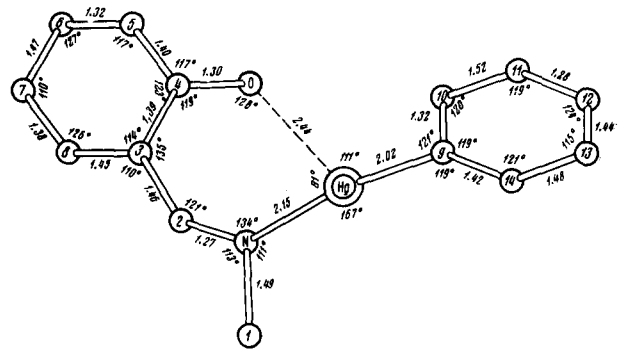


Figure 5.

A similar type of coordination of the mercury atom is found in 2-hydroxy-5-methylphenylmercury 4-methyl-2-nitrosophenoxide $C_7H_7OHg.C_7H_6ONO$ [42,43] (Fig. 6*a*). As in the preceding structure, the mercury atom is covalently bound through a carbon atom of the phenol ring and the nitrogen atom of the quinone monoxime. The unit cell contains two independent molecules, with mean Hg–N and Hg–C distances 2.14 and 2.04 Å. The C–N and N–O bonds (mean lengths 1.25 and 1.27 Å) are nearly double, since the molecular structure is best described by formula (II) (Fig. 6*b*).

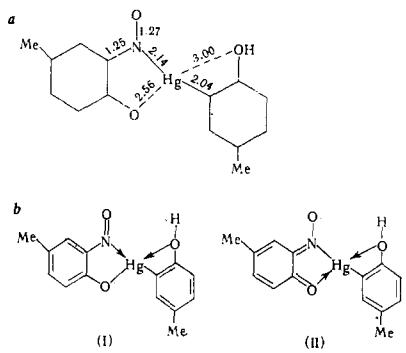


Figure 6.

The oxygen atom of the nitrosophenol is distant 2.56 Å from the mercury atom, which corresponds to coordination, but weaker than in phenylmercury *o*-methyliminomethylphenoxide. The probable reason for the weaker interaction is that a more symmetrical arrangement of the coordinated oxygen atom relative to the C–Hg–N fragment is

prevented by the geometrical rigidity of the five-membered "metal ring". The $O_{(1)}HgN$ and $O_{(1)}HgC$ angles are 71° and 115°, whereas in the salicylic derivative they are 81° and 111° respectively. The $N_{(1)}HgC$ angle away from the $O_{(1)}$ atom has also diminished to 174°. It is remarkable that a five-membered metal ring is formed in this structure, although the ligand is isoelectronic with salicylicidenimine, and on coordination of the mercury, not with the nitrogen but with the oxygen of the nitroso-group, would have formed a six-membered chelate metal ring analogous to that found in the above phenylmercury derivative of salicylicidenimine.

In all the above structures a shortening of the distance between the "additionally" coordinated heteroatom and mercury is sufficient to indicate interaction between these atoms without further corroboration. However, this is by no means always possible, and additional geometrical criteria of coordination must be used for such cases. They may be the deviation from the ideal XHgX angle opposite the "extra" atom, the symmetry of the position of the latter relative to the X–Hg–X fragment, and also the occurrence in the molecule of a conformation favourable to such interaction[44].

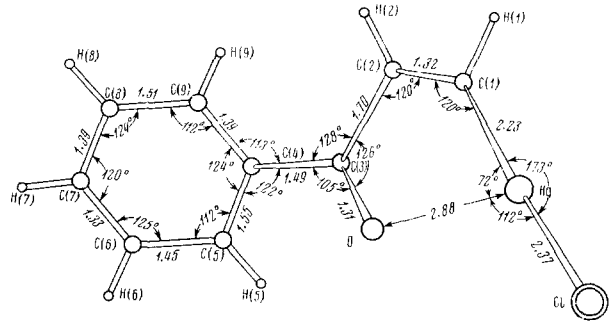


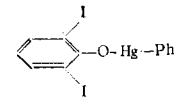
Figure 7.

An example is 2-benzoylvinylmercury chloride, whose *cis*-isomer was more stable than the *trans*-isomer, which was attributed[45] to intramolecular Hg...O coordination. X-Ray structure determination established a cisoid conformation[46] (Fig. 7), in which the oxygen atom lay in the direction of the mercury atom. The Hg...O distance of 2.88(10) Å agreed within the limits of accuracy with the sum of the van der Waals radii (2.9–3.1 Å). However, the molecular conformation and the diminution to 173(2)° in the ClHgC angle opposite the oxygen atom are evidence of the above coordination.

Examination of *cis*-2-chlorovinylmercury chloride by gas-phase electron diffraction[47] gave Hg–C and Hg–Cl bond lengths (2.14(1) and 2.27(1) Å) that can be regarded as normal. The non-bonded intramolecular Hg...Cl distance is 3.27 Å, and the sum of the van der Waals radii 3.3–3.5 Å. This distance was regarded as corresponding to intramolecular coordination. However, it is determined in considerable measure by the geometrical rigidity of the molecule, and cannot be used as an unequivocal criterion of coordination. Such interaction might be indicated by a decrease in the CHgCl angle away from the "extra" chlorine atom. Linearity of the C–Hg–Cl fragment is in fact disturbed (the angle is 168.5(1.5)°), but the side to which the Hg–Cl bond is deflected is not stated. The presence of coordination in this molecule is supported also by results obtained by other methods (dipole moments, anomalies of chemical behaviour, nuclear quadrupole resonance spectra)[48–50].

Only the coordinates of the mercury and halogen atoms have objectively been established in the crystal structure of trichloromethylmercury bromide CCl_3HgBr.[51] The Hg...Cl distances were not equivalent: two were 3.21 Å, and one 3.15 Å, the decrease being attributed to coordination. However, the poor accuracy does not allow this conclusion to be accepted as entirely reliable. Nevertheless, the presence of interaction is indicated by the nuclear quadrupole resonance spectra of trichloromethylmercury bromide and chloride and of bistrichloromethylmercury.

The Hg...I distance in the crystal structure of phenylmercury 2,6-di-iodo-4-methylphenoxide



was determined[52,53] as 3.14 Å, which corresponds to strong intramolecular coordination.

4. Crystal Structures of Organomercury Compounds with Intermolecular Coordination of the Mercury Atom

Coordinative saturation of mercury can be attained not only by the intramolecular interaction with the heteroatom discussed in the preceding subsection but also by interaction with donor atoms of a neighbouring molecule in the crystal.

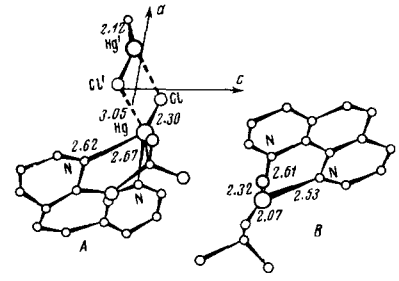


Figure 8.

X-Ray structure determination on the adduct of trichloromethylmercury chloride and 1,10-phenanthroline[54] indicated strong interaction between the mercury atom and the nitrogen atoms of the phenanthroline, with substantial disturbance of the linearity of the C–Hg–Cl fragment. The crystal structure contains two independent molecules A and B differing in geometry (Fig. 8), with CHgCl angles of 155° and 145° respectively. With such considerable disruption of the linear geometry of the mercury atom the Hg–C and Hg–Cl bond lengths—2.12 and 2.30 Å in A, and 2.07 and 2.32 Å in B—are almost the same as in linear

molecules. The Hg...N distances are 2.62 and 2.67 Å in A, and 2.53 and 2.61 Å in B. Coordination of the mercury atom in molecule B in the crystal conforms to a distorted tetrahedron; in A the additional effect of the close intermolecular Hg...Cl contact of 3.05 Å brings the coordination to distorted trigonal-bipyramidal.

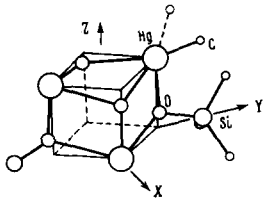


Figure 9.

Strong distortion of the linear geometry of the mercury atom has been found in methylmercury trimethylsiloxide[55]. The molecules are associated into tetramers (Fig. 9) having a cubane-like structure intermediate between the ideal cubane structure in the corresponding zinc and cadmium compounds (see below) and a structure with isolated molecules. Within the limits of accuracy the Hg–C and Hg–O distances of 2.09(40) and 2.11(20) Å correspond to normal covalent bonds in linear mercury molecules; the OHgC angle is 112(8)°. Thus even in this compound disturbance of the linear geometry of mercury is not accompanied by increase in Hg–O and Hg–C bond lengths. The coordination of mercury in the tetramer is supplemented by weak Hg...O interactions at distances of 2.75(20) Å to give a distorted tetrahedron. The arrangement of the methyl group attached to the mercury atom is random.

Several crystal structures have been described in which Hg...X coordination is achieved with considerably less distortion of the linear bond configuration of the mercury atom.

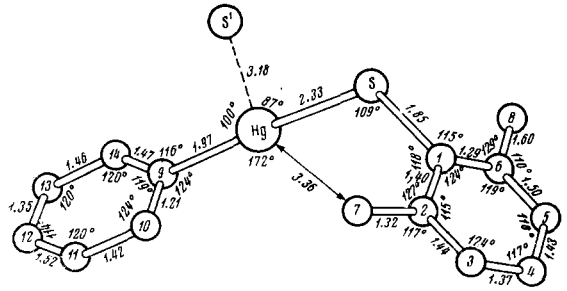


Figure 10.

An X-ray examination of phenylmercury 2,6-dimethylphenyl sulphide[44] had the aim of refining the van der Waals radius of the mercury atom, since intramolecular contact between the mercury atom and an electrically neutral methyl group should be present in this compound (Fig. 10). The Hg–C and Hg–X bond lengths are respectively 1.97 and 2.33 Å, and the SHgC angle is 172°. The angle between the HgSC(ω) plane and the plane of the thiophenol ring is 52.3°, with the mercury atom approaching a methyl group to 3.36 Å. On the assumption that contact occurs between the mercury atom and the carbon atom of the methyl group, whose hydrogen atoms do not prevent such contact, the van der Waals radius of the mercury atom is found to be ~ 1.6 Å, which lies between the two values suggested earlier[2]. The crystal structure involves intermolecular Hg...S′ coordination at 3.18 Å, which is 0.1–0.3 Å closer than the sum of the van der Waals radii. Such coordination is evidence also that the CHgS angle away from the S′ atom has decreased to 172° and that this atom is in a symmetrical position with respect to the C–Hg–S fragment. Furthermore, the angle at the sulphur atom (109°) is larger than the corresponding angle (100°) in the crystal structure of triphenyltin 2,4,6-trimethylphenyl sulphide[56], which may be due to a redistribution of electron density on the sulphur atom when it interacts with the mercury atom.

A similar increase in the angle at the sulphur atom (to 111°) was found in the crystal structure of mercury dimethanethiolate $(CH_3S)_2Hg$,[57,58] where intermolecular Hg...S interaction occurs at 3.25 Å, whereas in the structure of mercury diethanethiolate $(C_2H_5S)_2Hg$,[59] where such interaction is evidently absent (Hg...S = 3.56 Å), the HgSC angle is smaller (106°). The presence of coordination in the methyl derivative is confirmed by its higher melting point than those of the ethyl and propyl sulphides (175° compared with 76° and 71°C).

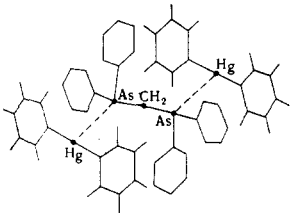
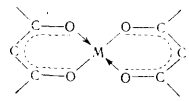


Figure 11.

The presence of Hg...As coordination has been established in the crystal structure of the 2 : 1 adduct of bispentafluorophenylmercury and bisdiphenylarsinomethane[60,61] (Fig. 11). The arsenic atoms are situated symmetrically with respect to the bispentafluorophenylmercury molecules: the AsHgC angles are 90(3)° and 96(3)°. The Hg...As distance of 3.40 Å is 0.1–0.3 Å less than the sum of the van der Waals radii, and the CHgC angle away from the arsenic atom has closed to 173(4)°. Further evidence of Hg...As interaction is that the angle between the planes of the pentafluorophenyl rings is 7°, whereas it is 59.4° in the crystal structure of bispentafluorophenylmercury (see subsection II, 2). Such a tendency of the latter molecule to achieve planarity in the adduct facilitates approach of the arsenic to the mercury atom.

X-Ray examination of bisdipivaloylmethylmercury has established[62,63] that the mercury atom, in contrast to the atoms of transition metals, which form chelate complexes



with dipivaloylmethane, is attached to the two central carbon atoms of the ligands (Fig. 12). Only one moiety of the molecule is involved in additional Hg...O coordination (in conformity with which the thermal vibrations are smaller in this half). Such interactions lead to a decrease (to 170°) in the angle away from the two interacting oxygen atoms, to a lengthening to 2,18(3) Å of the Hg–C bond in the moiety involved in interaction (the length of the second Hg–C bond is 2.13(3) Å), and also to an increase to 120° of the angle at the central carbon atom in this moiety, which indicates a contribution by the sp^2 state of this atom.

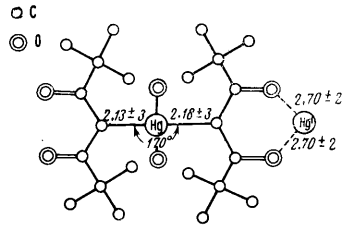


Figure 12.

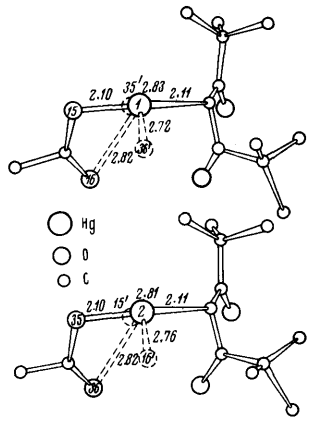


Figure 13.

In the crystal structure of dipivaloylmethylmercury acetate[64] the mercury atoms of two crystallographically independent molecules are involved in intermolecular coordination with oxygen atoms of acetate groups (Fig. 13): the oxygen atoms of the dipivaloylmethyl groups play no part in these interactions. The intramolecular Hg...O distances vary between 2.72 and 2.83 Å. The intramolecular Hg...O distance to the second oxygen atom of the acetate group (2.82 Å) is determined by the geometrical rigidity of the HgOCO fragment, so that we do not know whether it corresponds to interaction. Fig. 14 shows the coordination polyhedron of the mercury atom. As in certain other cases in which mercury is coordinated with more than two atoms corresponding to a more complicated polyhedron, the criterion of a decrease in bond angle at the mercury atom is ineffective or completely unsuitable.

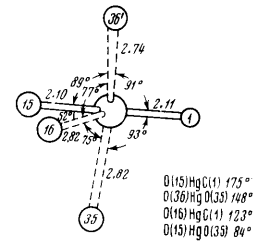


Figure 14.

A similar situation is found in the crystal structure of phenylmercury acetate[65] (Fig. 15). The Hg–$O_{(1)}$ and Hg–$C_{(1)}$ bond lengths are respectively 2.11 and 1.92 Å, and the OHgC angle is 170°. The distance to the second atom of the acetate group $O_{(2)}$ is 2.85 Å, but here, too, the question of intramolecular interaction is evidently unsettled. In the crystal the mercury atom is surrounded by oxygen atoms of neighbouring molecules at distances of 2.94, 2.95, and 3.11 Å. Although these distances coincide with the sum of the van der Waals radii (2.9–3.1 Å), the fairly symmetrical arrangement particularly of oxygen atoms about mercury in a plane approximately perpendicular to O–Hg–C suggests that they are responsible for coordination interactions. The original authors regard them as van der Waals contacts.

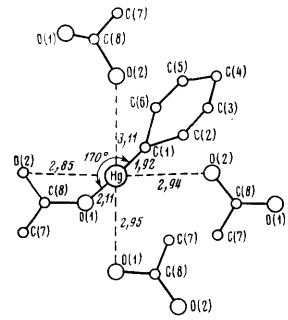


Figure 15.

An X-ray structure determination on 2-diethylaminoethylmercury chloride $(C_2H_5)_2N.CH_2.CH_2.HgCl$ was undertaken[66] to establish intermolecular Hg...N coordination in compounds of this type. The Hg–C and Hg–Cl bond lengths are 2.12 and 2.36 Å respectively. Coordination of the

mercury atom in the crystal is trebled by interaction with a nitrogen atom of a neighbouring molecule at 2.77(2) Å, with a decrease in the CHgCl angle to 173°.

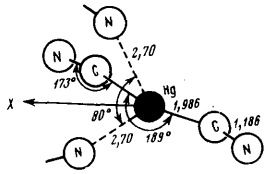


Figure 16.

X-Ray structure determination[67] and neutron diffraction[68] have given a closely similar intermolecular Hg...N distance in the mercury(II) cyanide crystal (2.70 and 2.74 Å). The former method shows that the CHgC angle away from the two coordinating nitrogen atoms (Fig. 16) has decreased to 171(2)°, and the Hg–C bond length is 1.986(16) Å. Neutron diffraction indicates that this angle is 175.0(2)°, and the bond length 2.015(3) Å. It is interesting to compare these results with those for methylmercury cyanide[13,14]. This molecule is linear, and the Hg...N distances (3.14 and 3.26 Å) are not shortened in the crystal. This is probably because replacing the cyanide group by methyl diminishes the positive charge on the mercury atom and weakens its ability to coordinate.

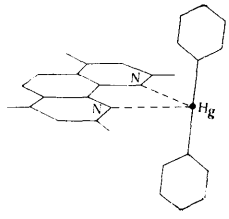
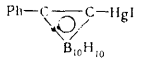


Figure 17.

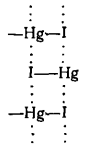
The crystal structure of the adducts of diphenylmercury with 2,9-di- and 2,4,7,9-tetra-methyl-1,10-phenanthroline[69] (Fig. 17) also show diminished coordinating power of mercury in the absence of electronegative substituents. One phenanthroline molecule is located near each diphenylmercury molecule in a plane approximately perpendicular to the C–Hg–C fragment and passing through the mercury atom (a second substituted phenanthroline molecule, not involved in contacts with the mercury atom, is also present). The Hg...N distances of 2.8–3.0 Å are greater in the two preceding structures, and close to the sum 2.8–3.0 Å of the van der Waals radii. Therefore coordination cannot be assumed on this basis alone, but its presence is suggested by such a specific relative arrangement of diphenylmercury and phenanthroline molecules.

X-Ray structure determinations on several barenyl derivatives of mercury halides[70] established the presence of strong intermolecular Hg...I interaction in phenylbarenylmercury iodide

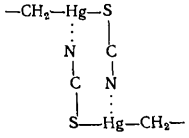


corresponding to 3.29 Å, which is 0.4–0.6 Å smaller than the sum of the van der Waals radii. Such interaction explains the spontaneous symmetrisation that occurs when the crystals are stored. Only the coordinates of the mercury and bromine atoms were determined in phenyl- and in methyl-barenylmercury bromide, and the Hg...Br distances shown to be respectively 3.42 and 3.56 Å, with the sum of the van der Waals radii 3.45–3.7 Å. However, the antiparallel arrangement of the Hg–Br fragments in the structure indicates weak intermolecular Hg...Br interaction.

Several crystal structures have been described in which the arrangement of heteroatoms in neighbouring molecules suggests the presence of coordination, although the atoms are no closer than the sum of the van der Waals radii. X-Ray examination of the compounds $CH_3O.C(CH_3)_2.C(CH_3)_2.CH_2.HgX$ showed[71] that, when X = I, the Hg–I bond length is 2.60 Å, and the intermolecular Hg...I distance 3.81 Å. Owing to weak intermolecular Hg...I interactions, infinite chains of antiparallel Hg–I fragments



appear in the crystal structure of this compound. In such compounds with X = SCN geometrical analysis of the coordinates of mercury and sulphur atoms reveals the formation of dimers



through the terminal nitrogen atoms of the thiocyanato-groups. The molecular configuration in the dimer corresponds to the isomer with closest approach of mercury and nitrogen atoms, probably as a consequence of coordination between them. Unfortunately, the Hg...N distances were not determined.

Intermolecular Hg..Cl interaction was established[72] in the crystal structure of 2-chlorovinylmercury chloride ClCH:CH.HgCl. The mercury atoms in three crystallographically independent molecules are coordinated by the chlorine atoms of neighbouring molecules; the Hg...Cl distances vary within the range 2.89–3.49 Å. The mean Hg–C and Hg–Cl bond lengths are respectively 2.10 and 2.30 Å. Unfortunately, no analysis of the coordinative environment of the mercury atoms is given in the paper.

X-Ray examination of phenylmercury halides established[73] that the Hg–Br bonds in the bromide have an antiparallel arrangement, with the mercury atom coordinated by four bromine atoms of neighbouring molecules (Hg...Br = 3.45 Å) in an octahedral environment. The Hg–C and Hg–Br bond lengths are 2.06 and 2.43 Å, and the CHgBr angle is 180°. The chloride and the iodide are isostructural with the bromide.

The crystal structures of *para*-derivatives of phenylmercury halides were also studied[74]. The coordinates of the mercury and chlorine atoms in *p*-tolylmercury chloride showed that the mercury atom is surrounded by three chlorine atoms of neighbouring molecules at 3.35, 3.35, and 2.99 Å. The packing of *p*-chlorophenylmercury chloride molecules in the crystal is closely similar to that of phenylmercury chloride, with a nearly antiparallel arrangement of Hg–Cl bonds. The tendency of the molecules to such an arrangement is so great that it is realised, although geometrical analysis shows that such packing will probably lead to the presence of closer intermolecular contacts.

An antiparallel arrangement of Hg–Br bonds was found also in *p*-tolylmercury bromide, in contrast to the corresponding chloride, and also leads to the presence of closer intermolecular contacts. This probably indicates that Hg...Br interaction is stronger than Hg...Cl interaction.

An antiparallel arrangement of Hg–Br bonds is impossible in the crystal structure of *p*-ethoxycarbonylphenylmercury bromide, containing a bulky *para*-substituent. The mercury atom in this crystal is surrounded by three bromine atoms of neighbouring molecules at distances 3.43, 3.43, and 3.55 Å (Hg–Br bond length 2.42 Å). *p*-Methoxyphenylmercury chloride, despite its large *para*-substituent, has the phenylmercury chloride type of crystal structure. This was explained by the "flexibility" of the methoxy-group, making it convenient for packing in the crystal.

III. ORGANOZINC AND ORGANOCADMIUM COMPOUNDS

The structures of the corresponding zinc and cadmium compounds have been studied considerably less than those of organomercury compounds. The reason is the great reactivity of the former, making their examination by X-ray or electron diffraction difficult.

The structures of dimethylzinc and dimethylcadmium, among organometallic compounds of type R_2M, have been studied by means of their Raman spectra[6]. Both molecules are linear. The Zn–C and Cd–C bond lengths are 1.929(4) and 2.112(4) Å, the latter thus being rather longer than Hg–C in dimethylmercury (2.094(5) Å). Thus the M–C bond length does not vary in parallel with the atomic number of the metal in the series zinc, cadmium, and mercury. A similar relation of bond lengths has been found for the dihydrides, in which the H–M distances in this series are 1.595, 1.762, and 1.740 Å. X-Ray examination of dimethylzinc[75] gave Zn–C = 1.96 Å, and a methyl group of a neighbouring molecule situated opposite the vacant *p*-orbitals of the zinc atom. This does not exclude weak interaction between them, like that observed in trimethylindium[75,76] and in trimethylaluminium[75,77].

Organozinc and organocadmium compounds in which the metal atom has a tetrahedral configuration are rather more stable, and have therefore been studied more thoroughly.

The crystal structure and the molecular structure of lithium tetramethylzincate were determined[78] by the powder method. The second of the two space groups $I\bar{4}2m$ and $I\bar{4}$, which differ in the orientation of the methyl groups, was chosen on the basis of crystallographic considerations. The zinc atom (Fig. 18) is located at a singular point on an inversion axis, and has distorted tetrahedral coordination. The Zn–C bond lengths of 2.07(15) Å were regarded as greater than the value of 1.929 Å in the linear molecule of dimethylzinc. However, the poor accuracy of this value does not permit the significance of such an increase to be assessed.

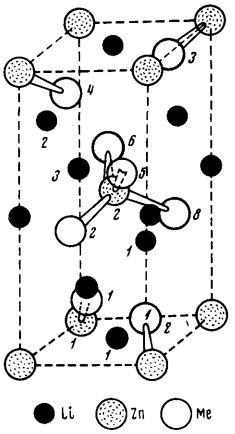


Figure 18.

Crystals of the isostructural potassium tetraethynylzincate and tetraethynylcadmate $K_2[Zn(C_2H)_4]$ and $K_2[Cd(C_2H)_4]$ have also been investigated by the powder method[79] (Fig. 19). In both compounds the metal atom has tetrahedral coordination. The $Zn–C_{(1)}$ distance of 2.0(1) Å was regarded as shortened by d_π–p_π interaction, although the poor accuracy evidently gives no grounds for such conclusions. The Cd–C distance is 2.5(1) Å.

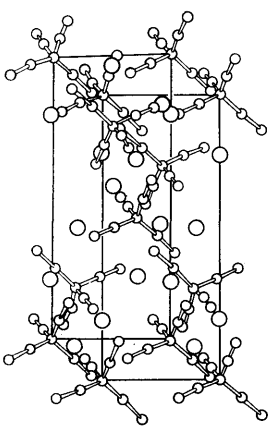


Figure 19.

The formation of tetra-, penta-, octa-, and poly-mers is very characteristic of organozinc and organocadmium compounds in the crystalline state. X-Ray examination of methylzinc methoxide[80,81] established the existence of a tetramer having a cubane structure (Fig. 20). Zinc and oxygen atoms occupy alternate corners of a distorted cube.

The Zn–C and Zn–O distances are 1.94 and 2.09 Å; the mean angles at the zinc and oxygen atoms are 83° and 96°.

On the basis of chemical and physicochemical investigations an analogous cubane structure was suggested[82-84] for the structurally unstudied compounds $[CH_3MOSi(CH_3)_3]_4$ (M = Zn, Cd) (Fig. 21) and $[CH_3ZnNP(CH_3)_3]_4$ (Fig. 22).

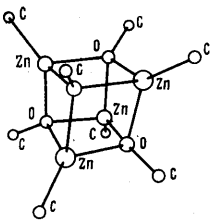


Figure 20.

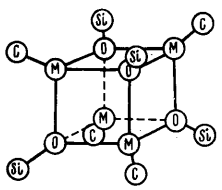


Figure 21.

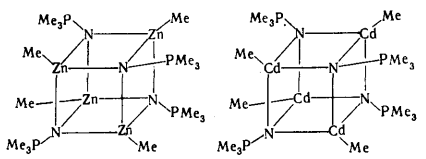


Figure 22.

X-Ray examination of the compound $Zn_7O_8(CH_3)_{14}$ shows[85] that it has a dicubane structure (Fig. 23) in which two kinds of zinc atoms differ in their coordination. The central zinc atom, located at a centre of symmetry, is octahedrally surrounded by methoxyl oxygen atoms at distances of 2.068–2.170 Å. The remaining zinc atoms have tetrahedral coordination with mean Zn–C distances of 1.953 Å, while the Zn–O distance varies between 2.026 and 2.147 Å.

The sulphur analogues—methylzinc isopropyl[86] and isobutyl[81] sulphides—have an interesting structure. The former is octameric (Fig. 24), but unfortunately the X-ray examination did not reveal the carbon atoms. The Zn–S distance varied in the range 2.161–2.489 Å. The zinc atoms in the latter compound (Fig. 25) are located at the vertices of a distorted square pyramid, and the sulphur atoms over the faces of this pyramid; bond lengths were not given.

Crystalline ethylzinc iodide does not have a tetrameric structure but is a coordination polymer[87,88] (Fig. 26), owing to the bulkiness of the iodine atom, which does not permit formation of a four-membered ring. This explains the difference in chemical behaviour (solubility in hydrocarbons) between this compound and the bromide and chloride, which have a tetrameric cubane structure in solution[89]. Nevertheless, the arrangement of zinc and iodine atoms is close to a cubane structure, which can be obtained (Fig. 27) simply by shifting two iodine atoms (as indicated by the arrows) in the four-membered fragment of the polymer. The zinc atom has a distorted tetrahedral coordination; the CZnI angle is 144.4(1.7)°, the Zn–C and Zn–I bond lengths are 1.95 and 2.64 Å, and the other two Zn–I distances to the iodine atoms of neighbouring fragments (C_2H_5ZnI) of the polymer are 2.91(6) Å.

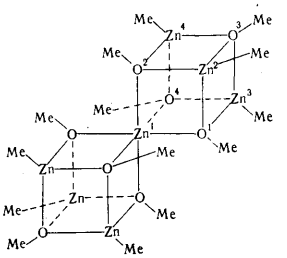


Figure 23.

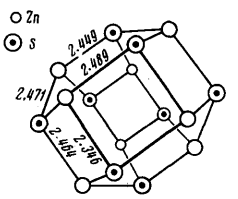


Figure 24.

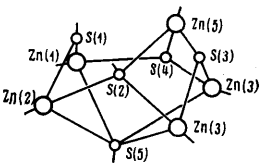


Figure 25.

The zinc atom in the crystal structure of the ionic methyldineopentylsulphonium tri-iododineopentylthiomethylzincate $[(C_5H_{11})_2SCH_3]^+[(C_5H_{11})_2SCH_2ZnI_3]^-$ is subject to distorted tetrahedral coordination[90] (Fig. 28) by three iodine atoms and one carbon atom. However, the Zn–I bonds have undergone more equalisation than in ethylzinc iodide (2.62, 2.63, and 2.68 Å), while the CZnI angle of 120°

shows maximum departure from the tetrahedral value; the Zn–C bond length is 2.14(3) Å.

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This Review shows that hardly any structural studies have been made on organic derivatives of zinc and especially of cadmium, mainly owing to the high reactivity of these compounds.

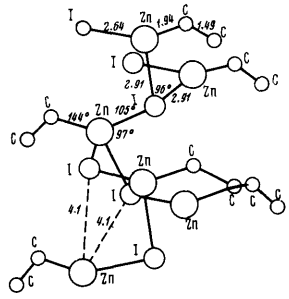

Figure 26.

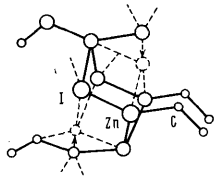

Figure 27.

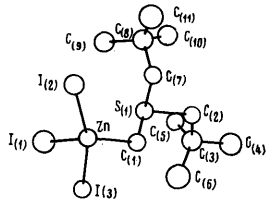

Figure 28.

The investigation of organomercury compounds, as already remarked, presents considerable difficulties owing to the great difference in atomic number between mercury and carbon. Only during recent years have papers appeared in which all the light atoms have been objectively revealed: in the vast majority of studies during the 1940s and 1950s either the coordinates of light atoms were not found at all or the accuracy of their determination was poor (~ 0.1 Å).

This aspect is especially significant in view of the fact that, in the investigation of organomercury compounds, interest lies not in establishing the structural formula, which usually requires no great accuracy, but in revealing weak intramolecular and intermolecular coordination interactions, whose analysis rests on fine changes in geometrical parameters (interatomic distances, bond angles). These interactions usually operate at large distances (~ 3 Å), close to the sums of the van der Waals radii. It is noteworthy, however, that the very concept of van der Waals radius was originally applied mainly to organogen elements, i.e. to non-metals and certain closely related classically non-transition elements (germanium, tin). However, the use of van der Waals radii of post-transition metals in which a *d*-shell has only just been filled, such as mercury, copper, etc., must evidently be approached with great caution.

The nature of the "additional" interactions discussed in the Review is not entirely clear. Electrostatic forces undoubtedly play an important part in many cases. However, it is difficult to explain the structure of many crystals, e.g. the adduct of diphenylmercury with phenanthroline, solely on the basis of electrostatic interactions. Not only further structural investigations but also appropriate quantum-chemical calculations are required to settle this question.

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Gel Chromatography of Condensed Phosphates

V.V.Pechkovskii, G.Kh.Cherches, and M.I.Kuz'menkov

The principles of the application of gel chromatography are discussed, together with its potentialities in the investigation of inorganic polymers of phosphorus with the aim of determining molecular dimensions, fractionating a mixture, obtaining individual phosphates, and also analysing their molecular-weight composition. The development and the achievements of the gel chromatography of condensed phosphates are surveyed. The phenomena occurring in a gel during the elution of inorganic compounds are described for several salts. A list of 91 references is included.

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III. Application of gel chromatography to the investigation of phosphates 91

I. INTRODUCTION

Molecular weight and degree of polydispersity are among the main characteristics of macromolecular compounds. Research has shown [1-6] that many properties of inorganic phosphate polymers depend directly on the size of the molecules. It is therefore very important to develop methods for investigating the molecular-weight composition of such polymers.

Almost all the methods known in the chemistry of macromolecular compounds—light scattering [1], ultracentrifuging [7,8], viscometry [1,9], chemical (end-group analysis) [10-12], and cryoscopic [13-15]—have been used to determine the mean molecular weight of condensed phosphates. Chromatographic methods of analysis (paper [16-18], ion-exchange [19-21], thin-layer [22-24], and electro-chromatography [25-27]) can be used to establish the molecular-weight distribution of polymers containing up to 10–14 phosphorus atoms in the chain. Precipitation [28-30] by means of various organic and inorganic reagents is, perhaps, the only method employed for the fractionation of macromolecular phosphates.

Promising new methods for isolating and separating condensed phosphates would contribute to further knowledge of their properties and structure. The production of porous gels varying in their permeability to molecules of different sizes was responsible for the rapid and widespread development of gel chromatography, a method of separation according to molecular weight†: since gel chromatography was first studied in 1959 on Sephadexes [31], more than 2000 publications have appeared on the application of the method.

Examples of hydrophilic gels used in gel chromatography are [32] dextrans—Sephadex (Sweden) and Molselekt (Hungary)—polyacrylamides—Bio-Gel P (USA) and Acrylex P (Hungary)—and agaroses—Sepharose (Sweden) and Bio-Gel A (USA). Organophilic examples include Sephadex derivatives and acrylic and polystyrene gels. Furthermore, dextran (ED, DED) and polyacrylamide (AM) hydrophilic gels and styrene—divinylbenzene (SDV) hydrophobic gels, similar in properties to the foreign products, have been manufactured in the USSR. [33] All the gels are produced as spherical granules of various sizes, and are divided into several types according to their porosity.

Gel chromatography was developed and used mainly for separating, isolating, purifying, and concentrating organic compounds, as well as for their molecular-weight analysis. A considerable number of reviews have been published on the theoretical basis of the method and its practical application in organic and biological chemistry [34-40].

The achievements and possibilities of gel chromatography have recently attracted the attention of inorganic chemists. The behaviour of halides, nitrates, sulphates, and perchlorates of alkali, alkaline-earth, and other uni- and bi-valent metals on Sephadexes and Bio-Gels has been investigated as a function of concentration, gel porosity, column height, eluent type, concentration, and pH, rate of elution, and temperature [41-52]. Gel chromatography has been used to study inorganic polymers such as phosphates [53-67], silicates [68], basic iron nitrates [69,70], and molybdates [71]. It has been employed to investigate complex formation with Trilon B [72,73] and other reagents [74,75]. Its application to the separation and investigation of various ions, complex compounds, and inorganic polymers has been reviewed [76,77].

These researches were decisive in establishing the processes occurring in a gel during the elution of electrolyte solutions. This knowledge served in turn as foundation for the practical application of gel chromatography to the determination of the sizes of ions, the separation and purification of inorganic substances, and the determination of the molecular-weight composition of inorganic polymers.

II. GEL CHROMATOGRAPHY OF INORGANIC COMPOUNDS

1. Processes occurring in the Gel during Elution

The solvent in a layer of a swollen gel can be regarded [34] as forming two phases—within and between the granules—so that the total volume of the layer can be expressed

(1)

where V_0 is the volume of solvent between the granules (external or free volume), V_i the volume of solvent inside the granules (internal volume), and V_m the volume of the

† The term *gel chromatography* is used in this Review as the most common in the chromatography of inorganic substances on gels.

gel matrix. Various phenomena may occur on the elution of dissolved molecules in such a system. Which phenomenon predominates is determined by the interaction of gel, solute, and solvent.

Numerous experimental results show that dissolved molecules are eluted from a gel chromatographic column in the order of their diminishing size or molecular weight. Such an inverse molecular-sieve effect is due to the fact that dissolved molecules of different sizes penetrate the swollen granules to different extents, which may be connected both with steric factors and with diffusion. The elution volume V_e of any solute is therefore intermediate between that of a substance which is completely excluded from the gel granules (equal to the free volume V_0) and the elution volume of a substance which is uniformly distributed between the two phases (equal to the total volume of solvent $V_0 + V_i$):

$$V_e = V_0 + K_d V_i, \qquad (2)$$

where K_d is the distribution ratio of the solute between the two solvent phases ($0 \leq K_d \leq 1$ in magnitude), which characterises the degree of penetration of solute inside the gel.

The above molecular-sieve mechanism is apparent in most cases of the gel chromatography of organic and inorganic substances; it is supported also by the consistency of experimental results with relations between elution parameters and molecular weights or sizes calculated on the basis of various models of gel structure [78-80]. However, several examples are known, especially in the elution of aromatic and heterocyclic compounds [81], their derivatives containing ionisable groups, and many inorganic salts [41], where the behaviour on gel chromatography cannot be satisfactorily explained solely by the molecular-sieve effect.

Secondary effects (secondary with respect to separation according to molecular weight, but in some cases decisive) are apparent in disturbances of the sequence of elution with diminishing molecular weight or size, in significantly overestimated ($V_e > V_0 + V_i$) or underestimated (in comparison with expectation from molecular size) elution volumes, in asymmetry of the chromatographic peaks, and in a dependence of the elution parameters on the concentration of the solute and on the nature and concentration of the eluent. These phenomena may result from specific interaction of the gel with certain substances and ions both in the separable mixture and in the eluent, as well as with their mutual complexes.

Abnormally high partition coefficients (or elution volumes) are a consequence of the retention of a substance in the column, owing to ion exchange or physical and chemical adsorption by the gel. The substance is then eluted by a volume of solvent exceeding $V_0 + V_i$, and the partition coefficient $K_d > 1$.

In several cases, on the other hand, substances are eluted from the column earlier than would be expected from their molecular size. This phenomenon, termed *ionic exclusion*, is attributed to the presence of a small quantity of negatively charged carboxylate groups in Sephadex, which repel solute anions, which are thus excluded from the gel granules and are eluted earlier.

Adsorption and ionic exclusion effects can be observed in the elution of sodium sulphate, chloride, nitrate, and perchlorate on Sephadex G-15 with 0.1 M sodium chloride solution [42]. The elution volumes of these salts increase in the sequence

$$Na_2SO_4 < NaCl < NaNO_3 < NaClO_4.$$

Sodium nitrate is eluted by a volume of solvent exceeding the total volume; the perchlorate is eluted still more slowly; and the partition coefficient of sodium sulphate (~0.1) is considerably smaller than the value to be expected from the radius of the hydrated sulphate ion [82]. Furthermore, experimental results on the elution of the chlorides of several metals with solutions of 0.1 M KCl + 0.01 M HCl, 0.1 M Na_2SO_4 + 0.005 M H_2SO_4, 0.1 M $NaNO_3$ + 0.01 M HNO_3, and 0.1 M $NaClO_4$ + 0.01 M $HClO_4$ on Sephadex G-25 showed that the partition coefficients of the metal ions in the nitrate and perchlorate systems were respectively 1.0–1.5 and 1.8–2.7, but those for the sulphate system were closely similar and small (up to 0.4). [43,44] These data indicate specific interaction between the gel and these ions, i.e. adsorption of nitrate and perchlorate ions and considerable exclusion of the sulphate ion.

Adsorption can be observed also in the elution of substances by eluents which by themselves are inert towards the gel. An example is the elution of zinc and cadmium chlorides on Sephadex G-10, which depends on the concentration of the eluting sodium chloride solution [45]: with increase in the eluent concentration chloride complexes are formed, whose adsorption on the gel produces values of $K_d > 1$.

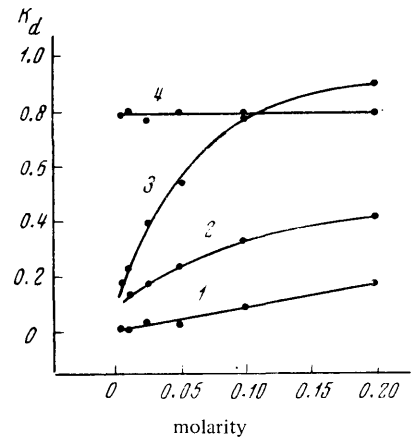

Figure 1. Effect of concentration of test material (in 50 ml of solution eluted with water on Sephadex G-10 at 35 ml h^{-1}) on its partition coefficient calculated from V_e, V_0, and V_i for [46]: 1) $Na_5P_3O_{10}$; 2) Na_2HPO_4; 3) NaCl; 4) glucose.

The ionic exclusion effect can be diminished by using a suitable eluent containing a supporting electrolyte to neutralise the action of the gel. Secondary effects are strengthened when water without a supporting electrolyte is used as eluent. In the elution of solutions of certain electrolytes with water, for example, their partition coefficients are relatively small and increase with the concentration of the solutions [46,47]. Use of an electrolyte as eluent increases the partition coefficients. The elution curves of non-electrolytes, e.g. glucose, do not depend on these factors (Fig. 1). To explain the processes occurring in a gel during the elution of electrolyte solutions the penetration of the supporting electrolyte into the interior of the gel phase was assumed to be incomplete owing to

steric and electrostatic factors[42,48]. Indications that part of the water involved in the swelling of a gel hydrates the polysaccharide chains of dextran[81] confirm the existence in the gel of a region which is inaccessible to dissolved molecules.

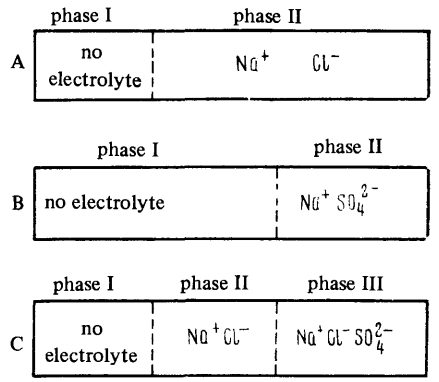

Figure 2. Diagram of distribution of ions in gel granules[42].

Thes properties of a gel are shown diagrammatically in Fig. 2. Their effect has been discussed in relation to the behaviour of magnesium ions in the $MgCl_2$–NaCl and $MgSO_4$–Na_2SO_4 systems[42]. If the supporting electrolyte, i.e. sodium chloride, penetrates inside the granules to only a limited extent, the interior of the gel is divided into two phases, as it were, distinguished by the presence or the absence of the given electrolyte (Fig. 2*A*). The degree of penetration by the electrolyte, i.e. the extent of phase (II), is determined mainly by the size of the larger ion. Since the effective ionic size increases from chloride through sodium to the sulphate ion, this phase will be smaller in the sulphate than in the chloride system (Fig. 2*B*). In a homogeneous sample–eluent system the efficiency of elution of magnesium ions will depend on the degree of penetration of the gegenion into phase (II), since the magnesium ion should be near its anion to preserve the electrical neutrality of the solution. In the chloride system the magnesium ions penetrate the gel to an extent determined by their size, since the chloride ion is smaller than the magnesium ion. In the sulphate system the penetration of magnesium ions is governed by the size of the sulphate ion, which is larger than magnesium. Thus the volume accessible to magnesium ions is smaller in the sulphate than in the chloride system. When a mixed solution of sodium chloride and sodium sulphate is used as eluent, the internal liquid phase is regarded as consisting of three regions (Fig. 2*C*), the additional phase (III) containing sodium, chloride, and sulphate ions. Since magnesium and sulphate ions interact to form complexes, penetration of the former into the gel will be determined by the relative sizes of phases (II) and (III). This may explain results obtained for the elution of magnesium chloride with solutions containing different ratios of sodium chloride and sulphate (Fig. 3).

It has already been stated that secondary effects are apparent also in the dependenee of the position and the shape of the elution curves on the concentration of the substance. The degree of asymmetry of the elution peak can be assessed by the ratio F/B,[46] where F and B are the distances from the ordinate for the peak to the ascending and descending portions of the curve measured at mid-height. For example, the effect of concentration on the elution volume and the symmetry of the peak has been investigated in the sample–eluent systems

$MgSO_4$–Na_2SO_4, $Mg(ClO_4)_2$–$NaClO_4$, $Mg(NO_3)_2$–$NaNO_3$[42], $MgCl_2$–NaCl, $SrCl_2$–NaCl, $BaCl_2$–NaCl[44].

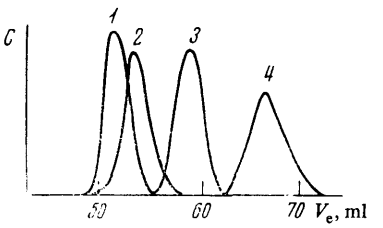

Figure 3. Variation of elution volume of Mg^{2+} ions from 0.01 M $MgCl_2$ (1 ml on Sephadez G-15 column 1.5 × 60 cm at 20–30 ml h^{-1}) with composition of eluent[42]: 1) 0.1 M Na_2SO_4; 2) 0.075 M Na_2SO_4 + 0.025 M NaCl; 3) 0.05 M Na_2SO_4 + 0.05 M NaCl; 4) 0.1 M NaCl; Here and on the other diagrams showing elution curves C denotes the relative concentration of the substance in the eluate.

Analysis of these results (Fig. 4) reveals three types of dependence of elution volume on concentration of the sample solution[44] according as $dV_e/d\lg[M]$ (i) vanishes (curves *1* and *2* at concentrations <0.1 M), (ii) <0 (curves *3*–*5* at <0.1 M and curve *6* at all concentrations investigated), and (iii) >0 (curves *1*–*5* at >0.1 M). In most cases the corresponding values of the ratio F/B were unity, <1, and >1.

These results reflect the processes occurring in the system. If a molecular-sieve mechanism alone operates, the elution curves are symmetrical, the partition coefficients are independent of concentration, and the relation $0 \leq Kd \leq 1$ is satisfied. With substances exhibiting symmetrical peaks at low concentrations and satisfying the above relation, the change in elution volume and in the shape of the peak with increase in concentration is attributed to diminished hydration of the ion and of the gel matrix with increase in the ionic strength of the solution, with a consequent increase in partition coefficient. Furthermore, the change in the degree of hydration may lead to the presence of hydrated ions of various sizes in the solution, whose elution curve will be non-Gaussian. A molecular-sieve mechanism then predominates. Asymmetry of the peaks and partition coefficients exceeding unity at low concentrations are a consequence of secondary processes.

2. Processing of Experimental Data and the Results of Gel Chromatography

Although the above secondary effects, representing an affinity for the gel phase, can sometimes be used for separation[34], the principal merit and the main use of gel chromatography consist in the relation between molecular

weight or size and the elution volume, which is possible when separation is due solely to a molecular-sieve mechanism. Various equations expressing the dependence of elution volume on molecular weight [34], "effective chain length" [83], Stokes radius [84], hydrodynamic volume [85], and molar volume [86] have been found for various substances. These equations contain parameters connected with the elution volume V_e/V_t and V_e/V_0, as well as partition coefficients, whose introduction permits comparison of results obtained with different columns and gels.

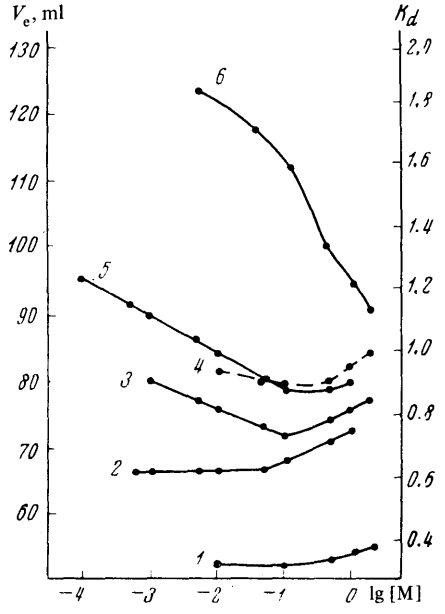

Figure 4. Dependence of elution volume and partition coefficient on sample concentration [M] (1 ml eluted at 20–30 ml h^{-1} on Sephadez G-15 column 1.5 × 60 cm with 0.1 M eluent) for the sample–eluent systems [42,44]: 1) $MgSO_4$–Na_2SO_4; 2) $MgCl_2$–NaCl; 3) $SrCl_2$–NaCl; 4) $Mg(NO_3)_2$–$NaNO_3$; 5) $BaCl_2$–NaCl; 6) $Mg(ClO_4)_2$–$NaClO_4$.

The partition coefficient characterises the behaviour of a substance in a gel, and a difference in its values for different substances may indicate differences in the mechanism of separation. From Eqn.(2) we have

$$K_d = \frac{V_e - V_0}{V_i} \qquad (3)$$

i.e. the free and internal volumes of the gel must be known in order to determine the partition coefficient. The former volume is determined by means of substances which are completely excluded from the gel and whose elution volume is $V_e = V_0$, while $K_d = 0$. A higher polysaccharide (dextran blue) and for inorganic systems a higher phosphate (e.g. Kurrol salt [53]) are most often used for this purpose.

The internal volume can be determined on the assumption that such compounds as hydrogen and sodium chlorides are uniformly distributed between the two phases, so that their elution volume $V_e = V_0 + V_i$ and $K_d = 1$. [46] The same hypothesis can be used to determine the internal volume for tritiated water THO. [53] However, comparison of the elution volumes of THO and $H_2^{18}O$ shows [87] that, owing to isotope exchange, the former has the rather larger elution volume. With the partition coefficient of the latter regarded as unity, those of tritiated water for Sephadexes G-10, G-15, and G-200 were determined as respectively 1.09, 1.06, and <1.02. [87]

In several cases the internal volume is determined by means of Eqn.(1), which gives

$$V_i = V_t - V_0 - V_m \ . \qquad (4)$$

The matrix volume of the gel is found from the specific volume of the latter (0.61). [88] The internal volume has been determined also [41] from the difference between the weights of the column containing the gel w, the empty column w_t, and the gel a transferred quantitatively from the column, washed with ethanol, and dried in a vacuum at 80°C for 6 h:

$$V_i = (w - w_t - a - \rho V_0)/\rho \qquad (5)$$

where ρ is the density of water.

In view of the presence in the gel of a region inaccessible to dissolved molecules, other workers [89] introduced the concept of an effective internal volume $(V_i)_{eff} = 0.8V_i$. It is advisable to use chloride and bromide ions—but not fluoride, iodide, sulphate, thiocyanate, copper(II), or iron(III)—for its determination.

Because of the uncertainty and difficulty of finding the internal volume, it is convenient to use the partition coefficient

$$K_{av} = \frac{V_e - V_0}{V_t - V_0} \qquad (6)$$

whose calculation depends on readily determinable quantities [80]. The relation between K_{av} and K_d is

$$K_{av} = K_d \frac{V_i}{V_i + V_m} \ . \qquad (7)$$

The difference in value between the two partition coefficients diminishes with increase in the porosity of the gel.

Partition coefficients are determined not only by the column method—i.e. under elution conditions—but also under static conditions [45,53,54]. The method is based on the postulate that the concentration of substances in the gel phase is the same as in the external liquid phase. Definite quantities of gel and solution of concentration C_1 of the substance in the eluent are stirred until equilibrium is established. After being allowed to settle, the concentration C_2 in the solution over the swollen gel is determined. We then have

$$K_d = 1 - \frac{V_0' + V_i'}{V_i'} \cdot \frac{C_2 - C_1}{C_2} \qquad (8)$$

where V_0' and V_i' are the free and internal volumes of the solvent. The sum $V_0' + V_i'$ is assumed to equal the volume of solution taken, and V_i' is determined by means of substances having $K_d = 0$.

Comparison of partition coefficients found by elution and under static conditions is used to estimate the contribution made by diffusion of the solutes to the separation [53,54]. Furthermore, the quantity $D = 100(C_1 - C_2)/C_1$ represents the contribution of adsorption, as a consequence of which $C_1 > C_2$ and $D > 0$. [45]

It was suggested[41] that the contributions of cation and anion to the partition coefficient of an ionic compound were additive:

$$K_d = \frac{s\Phi_c + t\Phi_a}{s+t} \qquad (9)$$

where t and s are the cationic and anionic charges, and Φ_c and Φ_a are the individual contributions of cation and anion to the partition coefficient. On the assumption that $\Phi_{Na} = 1$, the relative values of Φ_c and Φ_a were determined by a method similar to that used to find radii in a crystal. Good agreement was obtained with experimental partition coefficients for several salts on Bio-Gel P-2.

The use of gel chromatography to determine molecular weights, polydispersity, and molecular dimensions involves relating these characteristics with the elution parameters and employing the resulting mathematical and graphical formulae as calibration. In practice the elution volume is in most cases a linear function of the logarithm of the molecular weight. The best method for plotting a calibration straight line is to use monodisperse fractions of the test polymer, since the relation between molecular weight and molecular size may differ substantially for each type of compound. In several cases, however, calibration lines are obtained by means of standard specimens, e.g. narrow fractions of polystyrene or proteins[34].

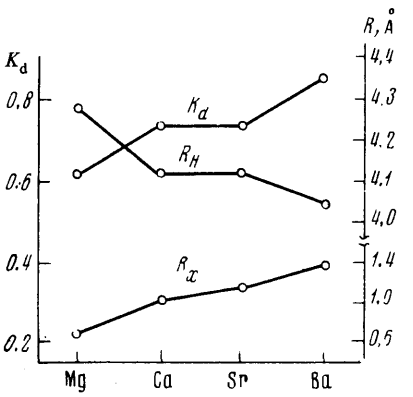

Figure 5. Comparison of partition coefficients and ionic dimensions of alkaline-earth metals[48] for 1 ml of 0.01 M solution eluted on Sephadex G-15 with 0.1 M NaCl + 0.01 M HCl at 20–30 ml h^{-1}: R_X = radius of ion in crystal; R_H = radius of hydrated ion.

The elution curve for the fractionation of a polydisperse polymer on an already calibrated column may be used to characterise its molecular-weight distribution. Analysis of the molecular weight and the quantity of each fraction obtained by preparative gel chromatography will also yield distribution curves.

Consideration of the various processes occurring during elution in a gel indicates that calibrations can be used to find ionic sizes or molecular weights when separation is due solely to a molecular-sieve mechanism. It is assumed that interactions among gel, substance, and eluent, apparent as adsorption, ionic exclusion, ion exchange, or complex formation, are absent.

The behaviour of inorganic salts in gel chromatography is in many cases consistent with a molecular-sieve mechanism. Comparison of the partition coefficients of alkaline-earth metal chlorides with the ionic radii, for example, shows (Fig. 5) that these salts are eluted in the sequence of diminishing size of the hydrated cations[48].

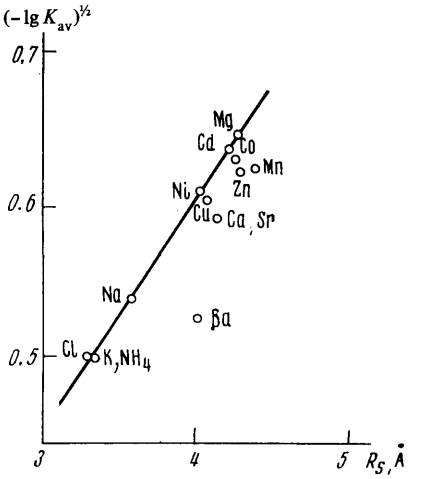

Figure 6. Relation between $(-\lg K_{av})^{1/2}$ and R_S for certain ions[43].

The model of a gel as a network of straight, rigid filaments, of infinite length and distributed at random in the gel[81], yields the relation

$$(-\lg K_{av})^{1/2} = A \cdot R_s + B \qquad (10)$$

between the partition coefficients and the radii R_S of dissolved molecules, where A and B are constants for a given gel. Fig. 6 illustrates the dependence of $(-\lg K_{av})^{1/2}$ on R_S for several ions eluted by 0.1 M potassium chloride solution on Sephadex G-15.[43] Results for ions which do not form chloride complexes and are not adsorbed on the gel lie on a straight line, which can be used as calibration for estimating the sizes of the ions.

The results given here illustrate the application of gel chromatography to the investigation of inorganic substances. It has been used to determine the sizes of various ions[43,48,72], as well as for the separation of ions[50–52] and the investigation of inorganic polymers. Information has been obtained on the properties of polysilicic acid[68], the existence of various types of polymeric molybdates[71], and the composition of $Fe(OH)_x(NO_3)_{3-x}$ polymers[69,70].

The rapid development of the application of gel chromatography to the investigation of inorganic polymers of phosphorus enables existing data to be generalised and further possibilities for the use of this method to be defined.

III. APPLICATION OF GEL CHROMATOGRAPHY TO THE INVESTIGATION OF PHOSPHATES

In order to establish rules for the gel-chromatographic behaviour of phosphates and to develop a technique, investigations were made on various individual phosphates [53–59], both linear and cyclic, and with different degrees of oxidation of the phosphorus, as well as specimens of polyphosphoric acids [58,60,61] and polyphosphates [62–67] having different molecular-weight distributions. Studies have been made of the effects of various factors on the behaviour of phosphates during chromatography—sample and eluent concentrations [55], pH, [54,55] rate of elution, temperature [57], gel porosity [55,57] and particle size [57], and the column parameters [57,58].

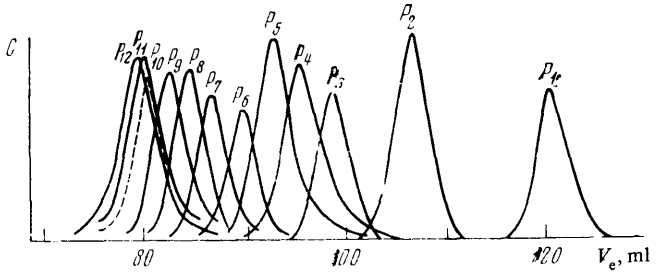

Figure 7. Elution curves for P_1-P_{12} linear polyphosphates [54] (1 ml containing 0.003–0.005 g-atom P litre^{-1} eluted on Sephadez G-25 column 1.5 × 90 cm with 0.1 M KCl of pH 7.0 at 20–30 ml h^{-1}).

Table 1. Partition coefficients of linear phosphates $Na_{n+2}P_nO_{3n+1}$ (0.003–0.005 g-atom P litre^{-1} eluted with 0.1 M KCl on Sephadex G-25).

P_n	K_d*	P_n	K_d	P_n	K_d	P_n	K_d
P_1	0.78	P_6	0.41	P_8	0.30	P_{12}	0.21
P_2	0.62	P_6	0.38	P_9	0.28	P_{13}	0.17
P_3	0.52	P_7	0.34	P_{10}	0.24		
P_4	0.46			P_{11}	0.23		

*Values of K_d for P_4-P_{13} phosphates calculated from those of K_{av}^{54}.

The concentration of phosphate in the eluate fractions was determined colorimetrically (Refs. 53–55 describe chemical analysis for phosphorus) and refractometrically with appropriate instruments, e.g. an interferometer [58] or a flow-type differential refractometer [57]. In the investigation of polyphosphoric acids, the pH of the eluate was measured by means of a pH-meter having a specially designed flow-type microcell [60,61]. The degree of polymerisation of phosphates in the eluate fractions was monitored by potentiometric titration [66,67] and by paper chromatography [58,60,65].

Many authors mention that phosphates are eluted from a gel column in the sequence of decreasing molecular weight. This relation has been found for linear phosphates containing 1–12 phosphorus atoms in the chain, eluted with 0.1 M potassium chloride solution on Sephadex G-25 [54] (Fig. 7), and for sodium ortho-, pyro-, and tripoly-phosphates on Sephadexes G-10, G-15, G-25, and G-50 [55] (Fig. 8). The partition coefficients of linear phosphates (Table 1) and of compounds containing up to four phosphorus atoms in different states of oxidation (Table 2) lie in the range $0 \leq K_d \leq 1$.

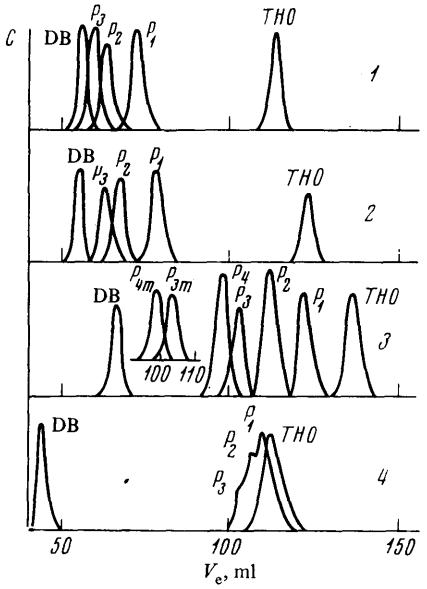

Figure 8. Elution curves of certain phosphates (1 ml of solution containing 0.002–0.005 g-atom P litre^{-1} eluted with 0.1 M KCl at 20–30 ml h^{-1}) on different Sephadexes [55]: 1) G-10 (column 1.5 × 90 cm); 2) G-15 (1.5 × 90); 3) G-25 (1.5 × 90); 4) G-50 (1.2 × 130). The peaks correspond to: P_1-P_4) polyphosphates containing a chain of 1–4 phosphorus atoms; P_{3m}) Na trimetaphosphate; P_{4m}) Na tetrametaphosphate; DB) dextran blue; THO) tritiated water.

Table 2. Effect of eluent concentration on partition coefficient K_d of phosphates [55]. (0.002–0.005 g-atom P litre^{-1} on Sephadex G-25).

Phosphate		Eluent			
formula	notation*	water	KCl solution		
			0.1 M	0.5 M	1.0 M
$NaPH_2O_3 \cdot H_2O$	P^1	—	0.80	0.83	0.83
$Na_2PHO_3 \cdot 5H_2O$	P^3	—	0.78	0.83	0.84
$NaH_2PO_4 \cdot 2H_2O$	P_1	0.36	0.78	0.83	0.84
$Na_3P_3HO_5 \cdot 12H_2O$	P^2-P^4	—	0.64	0.74	0.76
$Na_2H_2P_2O_6 \cdot 6H_2O$	P^4-P^4	—	0.67	0.77	0.79
$Na_3P_3H_2O_8$	P^3-O-P^3	—	0.59	0.66	0.69
$Na_3P_3HO_8 \cdot 4H_2O$	P^3-O-P^5	—	0.61	0.70	0.73
$Na_4P_2O_7 \cdot 10H_2O$	P_2	0.30	0.62	0.71	0.75
$Na_5P_3O_8 \cdot 14H_2O$	$P^4-P^3-P^4$	—	0.61	0.73	0.76
$Na_4P_3HO_8 \cdot H_2O$	$P^3-O-P^4-P^4$	—	0.50	0.62	0.70
$(NH_4)_5P_3O_9 \cdot xH_2O$	$P^5-O-P^4-P^4$	—	0.51	0.67	0.70
$Na_5P_3O_{10} \cdot 6H_2O$	P_3	0.21	0.52	0.62	0.69
$Na_3P_3O_9 \cdot 6H_2O$	P_{3m}	—	0.52	0.67	0.70
$Na_6P_4O_{11} \cdot xH_2O$	$P^4-P^4-O-P^4-P^4$	—	0.46	0.62	0.64
$Na_4P_4O_{10} \cdot 4H_2O$	$(-P^4-P^4-O-)_2$	—	0.48	0.62	0.65
$Na_4P_4O_{12} \cdot 4H_2O$	P_{4m}	—	0.46	0.60	0.65

*The superscript indicates the state of oxidation of the phosphorus, and the subscript the degree of polymerisation of the polyphosphate or metaphosphate (n_i).

The above results—the elution sequence, partition coefficients, and the symmetry of the peaks—are consistent with ideas on the sizes of polyphosphate anions and indicate that the mechanism of separation is based solely on a molecular-sieve effect.

Cyclic tri- and tetra-metaphosphates are eluted on Sephadex G-25 together with linear phosphates[55] (Fig. 8) according to their size.

Investigation of the dependence of the gel-chromatographic behaviour of polymeric phosphates on various factors has enabled important problems of technique to be solved and the most suitable parameters to be selected, whose use ensures the necessary conditions for a molecular-sieve mechanism to operate and for condensed phosphates to be analysed by means of calibration curves.

The availability of gels differing in porosity makes possible the analysis of polymers over a wide range of molecular weights. In the case of organic compounds limits have been found to the molecular weights, which are characteristic of each type of gel[34]. These limits may be different for inorganic substances, since other factors may then become more significant—ionic exclusion and hydration, and with phosphates the properties resulting from their polyelectrolyte nature.

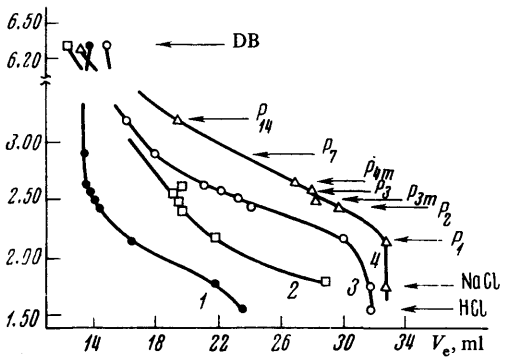

Figure 9. Dependence of relation between logarithm of molecular weight M [of phosphate] (eluted with 0.01 M NaCl) on gel porosity for columns 0.61–0.62 cm in diameter and 120–126 cm in height[57] of: 1) Sephadex G-10; 2) Bio-Gel P-2; 3) Sephadex G-25 (eluent 0.025 M Na_2HPO_4); 4) Sephadex G-50.

When an inhomogeneous sample of sodium polyphosphate of mean degree of polymerisation $\bar{n} = 14$ was eluted on Sephadexes G-25 and G-50, the partition coefficients of the component polyphosphates were closely similar and approached zero on Sephadex G-25, but distribution occurred throughout the accessible volume on G-50.[57] However, other factors—nature and concentration of eluent, quantity of sample solution—were not constant in this comparison. The shift in elution volumes and the difference in quality of separation characteristic of gels of different porosities are well illustrated by Figs. 8 and 9,[55,57] which show that the most satisfactory separation of oligophosphates is attained on Sephadex G-25.

The eluent may have a significant effect on the distribution of inorganic substances during elution. The influence of the supporting electrolyte on the separation of phosphates has also been studied. The partition coefficients of ortho-, pyro-, and tripoly-phosphates eluted with water on Sephadex G-25 are extremely low compared with the values obtained when potassium chloride solutions are used as eluent[55] (Table 2). The low values were explained by ionic exclusion, which is eliminated by the addition of potassium chloride to the eluent, for which purpose an electrolyte concentration <0.01 M was sufficient. The partition coefficients for anions with different states of oxidation of phosphorus increased slightly with the potassium chloride concentration (Table 2). Several explanations are possible for this effect: since polyphosphates possess the properties of polyelectrolytes, the size of their polyanions should diminish with increase in the ionic strength of the solution; another possible cause would be a decrease in the degree of hydration of the anions; furthermore, preliminary experiments showed[55] that the internal volume of Sephadex G-10 increased with the potassium chloride concentration of the eluent.

Examination of the behaviour of alkaline-earth metal chlorides in 0.1 M NaCl and 0.1 M NaCl + 0.01 M HCl showed[48] that the acid eluent gave the best separation. Such an eluent is undesirable with phosphates, owing to the increased probability of hydrolysis. The effect of the pH of the eluent on the partition coefficients was therefore examined. With linear phosphates[54] no appreciable changes in partition coefficients were observed with eluents having pH 2.0, 4.6, 7.0, and 9.2, obtained by adding respectively aqueous hydrochloric acid and phthalate, tris, and ammoniacal buffers to 0.1 M potassium chloride solution. Similar results were obtained in the separation of anions in which phosphorus was present in different states of oxidation[55]. Only on the addition of borate buffers of pH 7.0 and 9.2 were the partition coefficients lower, owing to electrostatic repulsion of phosphate ions and borate ions retained by the gel, which were able to interact with dextran depending on the pH.[90] The results confirmed yet again the need for careful choice of eluent if molecules are to be separated by a molecular-sieve effect.

Table 3. Dependence of partition coefficients K_d on concentration of sample[55] (on Sephadex G-25 eluted with 0.1 M KCl).

Phosphate*	Concentration, g-atom P litre^{-1}						
	0,001	0,005	0,01	0,05	0,1	0,5	1,0
P^3	0.78	0.78	0.78	—	0.79	—	0.80
P_1	0.78	0.79	0.79	—	0.80	—	0.80
P^4—P^4	0.66	0.66	0.66	0.69	0.71	—	—
P_2	0.62	0.63	0.63	—	0.69	—	—
P_3	0.52	0.50	0.51	0.55	0.57	0.66	0.70
P_{3m}	0.52	0.52	0.52	—	0.58	—	0.69
P^4—P^4—O—P^4—P^4	0.46	0.46	0.46	—	0.50	—	0.66
(—P^4—P^4—O—)$_2$	0.48	0.48	0.47	—	—	—	—
P_{4m}	0.46	0.46	0.45	—	0.50	—	0.63

* Notation as in Table 2.

In order to confirm the molecular-sieve mechanism it is necessary to determine the effect of the concentration of the test substances on their partition coefficients and the symmetry of the peaks. Table 3 lists values of K_d for certain phosphorus-containing compounds as a function of their concentration.

Fig. 10 illustrates the concentration dependence of the position and form of the elution peaks for sodium tripolyphosphate. With a sample concentration below 0.01 g-atom P litre^{-1} the elution curves are symmetrical, and the position of the peak remains unchanged. At higher concentrations the curves are displaced towards large volumes, and the peaks become unsymmetrical with $F/B > 1$. This was attributed to the presence of phosphate ions having different degrees of hydration. Furthermore, increase in the concentration of the polyphosphate is accompanied by a decrease in its dissociation[91], which with polyelectrolytes leads to a decrease in size of the polyanions. Similar results were obtained[57] for the effect of concentration on the elution parameters of sodium ortho-, pyro-, and tripoly-phosphates.

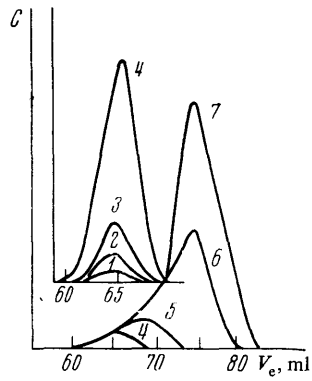

Figure 10. Dependence of elution curves for 1 ml of $Na_5P_3O_{10}$ (1.5 × 60 cm column of Sephadex G-25 eluted with 0.1 M KCl at 20–30 ml h^{-1}) on initial concentration[55] (g-atom P litre^{-1}): 1) 0.001; 2) 0.005; 3) 0.01; 4) 0.05; 5) 0.1; 6) 0.5; 7) 1.0.

Many authors state that the process becomes more efficient the longer the column, and this holds also for phosphates. The use of longer columns leads to a larger difference between the elution volumes of neighbouring polymer homologues and to better resolution of the peaks[58], but is accompanied by broadening of the curves, which has an adverse effect. Columns of height 60 and 500 cm give the same partition coefficients in the chromatography of a mixture of sodium ortho-, pyro-, and tripoly-phosphates on Sephadex G-25 with 0.01 M sodium chloride solution. The dependence of the elution of phosphates on the column parameters is obviously general in character.

In order to find the best conditions for the separation of substances a study was made[57] of the effect of various parameters on the resolution R of the peaks, defined by the equation

$$R = \frac{2(V_{e_2} - V_{e_1})}{w_{b_1} - w_{b_2}} \qquad (11)$$

in which the V_e are the elution volumes of adjacent peaks, and the w_b are their widths at the base. The resolution of sodium orthophosphate and tripolyphosphate is somewhat improved (Table 4) on decreasing the rate of elution, as a consequence of the diminished spreading of the bands. Raising the temperature has the opposite effect.

Completing our review of the different factors influencing the gel chromatography of phosphates and the techniques used, we can conclude that, within the limits investigated and allowing for actual applications, all the experimental conditions can be used for the gel chromatography of phosphates for analytical and preparative purposes.

Table 4. Effect of various factors on resolution R of $Na_5P_3O_{10}$ and Na_2HPO_4 peaks[57].

Experimental conditions		R
constant	variable	
Column dimensions, cm	Gel type	
diameter 0.61–0.62	Sephadex G-10	1.09
height 123.0–125.0	Sephadex G-25	1.47
	Sephadex G-50	1.35
	Bis-Gel P-2	0.87
Sephadex G-10 column, cm	Gel particle diameter, μm	
diameter 0.61	53–74	1.09
height 124.0–126.0	88–105	0.84
Sephadex G-25 (53–64 μm) (0.61 × 63.0 cm)	Rate of elution, ml min^{-1}	
temperature 22.0°C	0.16	1.69
	0.58	1.26
rate of elution 0.58 ml min^{-1}	22.0°C	1.26
	50.0°C	1.17

As mentioned earlier, various processes occurring in a gel as a result of interactions among the gel, test substance, and eluent affect the elution volumes (or partition coefficients), the elution sequence, the shape of the peak, and the dependence of these factors on the concentration of the substance. Investigations on phosphate polymers have shown that phosphates are eluted in the sequence of diminishing molecular weight, and that their partition coefficients in various gels lie in the range 0–1 and are constant with symmetrical curves over a certain concentration range. These results indicate the absence of interaction between phosphates and dextran. Furthermore, the identity of partition coefficients found under elution conditions and under static conditions indicates the absence of a diffusion contribution[53,54].

All the above facts indicate that, under certain conditions, the behaviour of phosphates on dextran gels is consistent with a molecular-sieve mechanism. It is therefore possible to use the method to separate and examine condensed phosphates, and important results in this field have already been obtained.

Firstly, it is now possible to obtain individual phosphates. When a solution of sodium polyphosphates having $\bar{n} = 3$, was fractionated on Sephadex G-15, components of a mixture with $n = 2-5$ were obtained in fairly pure form, isolated from the solution, and identified by paper chromatography and infrared spectroscopy.

Another important achievement of the application of gel chromatography to the investigation of phosphorus polymers is determination of the effective radii of many phosphate anions[54,55]. The radii were determined by means of a calibration line plotted from values of K_{av} and K_s for several ions, analogous to that shown in Fig. 6. The partition coefficients of the phosphorus-containing anions were calculated by means of Eqns. (6) and (7) with $V_i/(V_i + V_m) = 0.862$ for Sephadex G-25. The results show (Table 5) that these anions are considerably hydrated in aqueous solution, and that their size increases with the degree of polymerisation.

Finally, gel chromatography has been successfully used to determine the molecular-weight composition of a mixture of polyphosphates. A sample of sodium polyphosphates having $\bar{n} = 36$ was fractionated on Molselekt G-25,[66] the molecular weight of the polyphosphates in the eluate was determined by potentiometric end-group titration[11], and molecular-weight distribution curves were plotted from the fractionation results (Fig. 11). The reliability of the fractionation results is confirmed by the equality of the mean degree of polymerisation of the initial specimen and the sum of the products of the mole fraction x_i and the degree of polymerisation n_i of the ith fraction:

$$\bar{n} = \Sigma x_i n_i \quad . \qquad (12)$$

Table 5. Anionic radii R_S of phosphates[54,55] obtained from $(-\lg K_{av})^{1/3} = A \cdot R_s + B$

Phosphate*	R_s, Å	Phosphate	R_s, Å	Phosphate	R_s, Å
P^1	4.3	$P^4—P^3—P^4$	5.7	P_5	7.2
P^3	4.4	$P^3—O—P^4—P^4$	6.6	P_6	7.6
P_1	4.4	$P^5—O—P^4—P^4$	6.4	P_7	8.0
$P^3—P^4$	5.5	P_3	6.4	P_8	8.3
$P^4—P^4$	5.5	P_{3m}	6.4	P_9	8.6
$P^3—O—P^3$	5.8	$P^4—P^4—O—P^4—P^4$	6.8	P_{10}	9.0
$P^5—O—P^3$	5.7	$(—P^4—P^4—O—)_2$	6.8	P_{11}	9.2
P_2	5.7	P_4	6.9	P_{12}	9.3
		P_{4m}	6.9	P_{13}	9.8

*For notation see Tables 1 and 2.

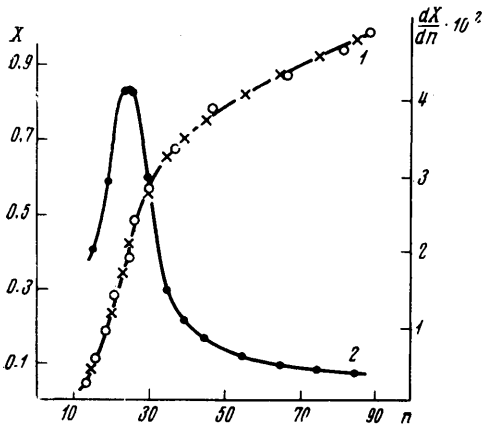

Figure 11. Numerical distribution curves for sodium polyphosphate with $\bar{n} = 36$ (0.5 g in 5 ml eluted on Molselekt G-25 column 1.3 × 80 cm with water at 26 ml h^{-1}):[66] 1) integral; 2) differential; ×) points chosen for graphical differentiation.

For the same purpose gel chromatography has been used to analyse a mixture of polyphosphates on Sephadex G-100.[67] Such investigations require a considerable quantity of the specimen, exceeding that at which the partition coefficient is still independent of concentration. Although a linear relation $V_e = k \lg M$ was obtained in these investigations, it can hardly be regarded as a calibration.

The calibration line (Fig. 12) for phosphates containing up to thirteen phosphorus atoms in the chain, determined by the use of individual phosphates obtained by ion-exchange chromatography[21], merits close attention in connection with the application of calibrated columns. Its possibility for calibration purposes was verified[54] by first determining by potentiometric titration the mean degree of polymerisation of a few polyphosphate specimens, and then chromatographing them on Sephadex G-25 with 0.1 M potassium chloride solution of pH 7.0. The concentration of the polyphosphates in each fraction was determined and also, from the calibration line, the degree of polymerisation, from which $\bar{n}$ in the initial specimen was calculated by a slightly modified form of Eqn. (12)

$$\bar{n} = \frac{\Sigma w_i}{\Sigma (w_i/n_i)} \qquad (13)$$

where w_i is the number of phosphorus atoms in the ith fraction. The good agreement between results obtained by the two methods showed the possibility of using this calibration (Table 6).

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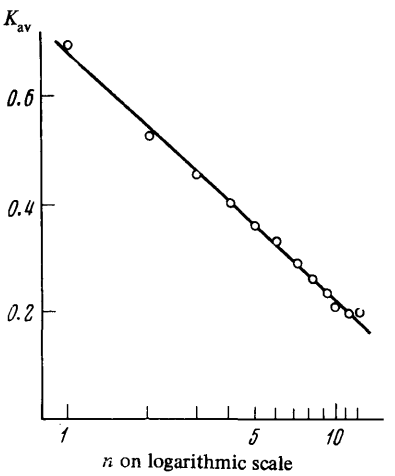

Figure 12. Relation between K_{av} and $\lg n$ for elution on Sephadex G-25 with 0.1 M KCl (pH 7.0) at 20–30 ml h^{-1}.[54]

Table 6. Comparison of mean degrees of polymerisation $\bar{n}$ of sodium polyphosphates obtained by gel chromatography and by potentiometric titration[54].

Method	$\bar{n}$					
Gel chromatography	3.2	8.4	9.3	9.5	12.0	14.0
Potentiometric titration	3.0	8.2	9.1	10.1	11.0	13.1

Gel chromatography has opened up new possibilities for the study of condensed phosphates. The achievements of the method, which was developed mainly for organic

chemistry, biochemistry, and clinical medicine, have proved useful for investigating inorganic phosphate polymers. The gel chromatography of phosphates has in turn confirmed several aspects of the method and has helped to expand its field of application.

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Sulphur Hexafluoride

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An attempt is made in the present review to arrange systematically the available data for the physicochemical and, primarily, chemical properties of sulphur hexafluoride. The inertness usually attributed to sulphur hexafluoride on the basis of early data obtained by Moissan hindered the investigation of its chemical properties. This gap is now being successfully filled. Data are presented showing that sulphur hexafluoride can serve as an effective fluorinating agent whose advantages are due to its high fluorine content, its non-toxicity, and the ease with which it can be handled. It is shown that further advances in the development of the chemistry of sulphur hexafluoride and of its practical applications depend significantly on the rate of development of research in this field.
The bibliography includes 236 references.

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I. INTRODUCTION

Metal and non-metal hexafluorides constitute a large and interesting group of fluorine-containing compounds, a distinctive feature of which is a strikingly wide variety of chemical properties, ranging from an extremely high reactivity to the inertness characteristic of noble gases[1-11]. Despite the fact that more than half of the members of this group of compounds were discovered as early as the beginning of the present century[12-19], their active study began only from the 1940's in connection with the preparation and employment of the hexafluorides of a number of elements in certain stages of the manufacture of nuclear fuel[20-24]. The eighteen hexafluorides known at present can be divided into two groups on the basis of their chemical behaviour: non-metal hexafluorides (SF_6, SeF_6, TeF_6, PoF_6 and XeF_6) and metal hexafluorides (CrF_6, MoF_6, TcF_6, RuF_6, RhF_6, WF_6, ReF_6, OsF_6, IrF_6, PtF_6, UF_6, NpF_6, and PuF_6). Whereas the former (with the exception of XeF_6 and PoF_6) are regarded as the most inert compounds, the latter exhibit a high activity, for example in fluorination or hydrolytic reactions.

Naturally this classification is extremely arbitrary and qualitative. Thus the reactivities of xenon and polonium hexafluorides resemble those of the most reactive metal hexafluorides. There is no doubt that the hexafluorides of iodine, astatine, and radon, which are so far unknown but are possible in principle, will not be chemically inert either.

Excluding XeF_6 and PoF_6, we may note that the chemical reactivities of the known non-metal fluorides increase in the sequence $SF_6 < SeF_6 < TeF_6$. For example, sulphur hexafluoride is inert with respect to hydrolysis by water vapour up to 500°C, while TeF_6 is fully hydrolysed by water in 24 h.

A similar situation obtains also for the lower chalcogen fluorides (tetrafluorides). Indeed the vigorously fuming liquid SeF_4 corrodes glass rapidly even at room temperature, solid TeF_4 readily reacts with quartz, while gases SF_4 is completely inert with respect to the latter. The chemical reactivities of the lower chalcogen fluorides served as a basis for their use as promising fluorinating and complex-forming agents.

On passing from the highest to the lowest fluoride of the same chalcogen, the chemical reactivity increases,

which is shown particularly clearly by sulphur compounds, for which the greatest number of lower fluorides is known [25-29].

Thus the sulphur pentafluoride dimer S_2F_{10} is more reactive than SF_6. On heating, it reacts with copper, mercury, and platinum and its reaction with iron takes place at room temperature. However, hydrolysis by water or concentrated alkalis is extremely slow. Sulphur tetrafluoride is very rapidly hydrolysed by water and sulphur fluoride (thiothionyl fluoride) S_2F_2 is hydrolysed even by atmospheric moisture.

Thus the above comparison shows that, among the nonmetal fluorides, sulphur hexafluoride is chemically the most inert. On the other hand, its high fluorine content (78%)—one of the most important parameters determining the effectiveness of any fluorinating agent—cannot fail to draw attention as regards the possible use of this compound in fluorination and oxidation processes, as pointed out at one time by Simons in his well known monograph [29]. The chemical inertness of SF_6 is an extremely arbitrary concept like the term "inert substance" in general.

The recent growth of interest in sulphur hexafluoride is due to its exceptional dielectric properties [30,31]. As data (mainly physical) accumulate, the range of practical applications of SF_6 is being extended, involving fields such as astronautics [32,33], electronics [34,35], refrigeration technology [36-39], meteorology [40-43], metallurgy [44,45], machine engineering [46], laser engineering [47,48], and medicine [49].

The available information about the chemical properties of sulphur hexafluoride has not changed significantly since the synthesis of this compound. A number of reviews [30,31,50], the latest of which is ten years old, contribute nothing new to the chemistry of sulphur hexafluoride compared with the information which was already available to Moissan. The gas which he isolated was very inert. Its hydrolysis by water vapour was not observed up to 500°C and it did not react with refractory glass up to the softening temperature of the latter. The gas did not react with halogens, phosphorus, arsenic, carbon, silicon, boron, copper, and silver at red heat. No reaction was observed between SF_6 and HCl or NH_3.

Sulphur hexafluoride is not acted upon by hot CuO and $PbCrO_4$ and by fused KOH. Only boiling sodium reacts rapidly and quantitatively with SF_6, which was used as a basis for the determination of the composition of this compound. A fairly large number of substances (large under the conditions prevailing at the time) had been tried in the reaction with SF_6, which enabled Moissan to characterise the hexafluoride as a chemically inert gas and to regard it as comparable to nitrogen in this sense. Thus there arose a seemingly well justified barrier, which determined the subsequent course of studies on the chemistry of this compound. Only in recent years new experimental data suggested ways of overcoming this largely psychological barrier in connection with certain advances in the chemistry of sulphur hexafluoride. A number of interesting reports dealing with the possibility of using SF_6 as a potential fluorinating and oxidising agent were published [51-59]. A number of studies by the authors of the review were directed to the same end [60-67]. It appears that further expansion of practical applications of sulphur hexafluoride will depend significantly on the rate of development of such investigations and therefore a survey of the accumulated data is an essential step in the development. This is why the authors of the review considered in greatest detail the advances in the investigation of the physicochemical and chemical properties of SF_6.

II. THE SYNTHESIS OF SULPHUR HEXAFLUORIDE

Sulphur hexafluoride is usually synthesised by the reaction of sulphur with gaseous fluorine [68-75]:

$$S + 3F_2 = SF_6 + Q \quad .$$

Depending on the apparatus employed and the purity of the starting materials, the product contains up to 5% of impurities in the form of lower sulphur fluorides (S_2F_2, SF_2, SF_4, and S_2F_{10}), oxide fluorides (SOF_2, SOF_4, and SO_2F_2), and dioxide (SO_2) as well as impurities introduced with the fluorine (HF, OF_2, CF_4, C_2F_6, N_2, and O_2). The gas obtained after purification is 99.8% pure and contains 8×10^{-6}% of $SF_4 + S_2F_2$ and 15×10^{-6}% of H_2O, S_2F_{10}, HF, and the inert gases being absent [31]. It is noteworthy that this gas is physiologically completely harmless [76].

Attempts were made recently to synthesise SF_6 without using elemental fluorine. This was done primarily by the electrolysis of sulphur or sulphur-containing compounds (H_2S, SCl_2, S_2Cl_2, and CS_2) in anhydrous hydrogen fluoride [77-80]. The processes [81,82]

$$6MF + S + 3Cl_2 = 6MCl + SF_6$$

or

$$3MF_2 + S + 3Cl_2 = 3MCl_2 + SF_6 \quad ,$$

where M is a Group I–IV metal, and the pyrolysis of lower sulphur fluorides [83] were considered as the basis for the possible methods of synthesis. However, both of the above reactions lead to the formation of a gas with a low sulphur hexafluoride content requiring careful purification.

Thus the method of synthesising sulphur hexafluoride based on the interaction of the elements still remains the one well tested and technologically and economically viable procedure. Nevertheless the synthesis of SF_6 on an industrial scale without the use of elemental fluorine appears to be very promising, since the available data suggest that this procedure is quite realistic.

Although the analytical chemistry of sulphur hexafluoride has not developed adequately [83-87], we may note that gas and gas–liquid chromatography appear to be the most useful in this field. The determination of impurities by this procedure has been sufficiently well developed [88-90]. The solid carriers employed are usually silica gel, Chromosorb W, or the "Kel-F" polymer with added fluorinated liquid hydrocarbons, among which poly(chlorotrifluoroethylene) is most frequently used.

III. PHYSICAL PROPERTIES

The Structure and Spectra

The first convincing evidence in support of the octahedral structure of SF_6 was obtained in electron diffraction experiments [91,92]. Six normal vibrations may be expected for a molecule with O_h symmetry, of which three [$\nu_1(A_{1g})$, $\nu_2(Eg)$, and $\nu_5(F_{2g})$] are active in the Raman spectrum and two [$\nu_3(F_{1u})$ and $\nu_4(F_{1u})$] are active in the infrared spectrum. There is also an inactive vibration in both spectra (ν_6), which may be observed as a combination band. All five absorption bands of gaseous and liquid sulphur hexafluoride were discovered as early as 1934, but the refinement of their positions by using better apparatus and purer specimens is still being continued (Table 1) [93-105].

The Raman spectra of solid and gaseous sulphur hexafluoride are very similar [94], which was in fact to be expected in view of the high symmetry of the molecule.

Table 1. The fundamental vibrational wavenumbers of SF_6 (cm^{-1}).

State of aggregation	$\nu_1(A_{1g})$ stretching vibration	$\nu_2(E_g)$ stretching vibration	$\nu_3(F_{1u})$ deformation vibration	$\nu_4(F_{1u})$ stretching vibration	$\nu_5(F_{2g})$ deformation vibration	$\nu_6(F_{2u})$
Gaseous	772.4 775 769.4 773.5	639.5 641.7	940 947 932 939 947 947.9	615 613 614 615	522 525	363 344 345 347

However, with the exception of the ν_1 line, other lines in the spectrum of solid SF_6 are weak and their assignment is extremely indefinite.

The absorption spectrum of SF_6 in the region of ultrasoft X-rays differs strongly from the usual X-ray spectra [106,107] and has a pronounced non-hydrogen-like character.

The electronic structure of the sulphur atom has been specified as $3s^{1.64}3p^{3.50}3d^{0.19}$, which leads to an effective charge of the sulphur atom of +0.67. [108] The experimental effective charge of the sulphur atom obtained by Coulson's method [109] proved to be 2.50. [110] The latter value is more accurate, since it was determined from the $K\alpha$ emission line, which corresponds to a more realistic redistribution of the electron density of sulphur. We may note that the involvement of d electrons in the formation of a chemical bond has been established also in a theoretical study of the electronic structure of SF_6 by the LCAO-MO SCF method [111]. A direct experimental confirmation of this finding was obtained by La Villa [112], who measured directly the probability of the $3d-2p$ transitions.

The photoelectronic spectrum of sulphur hexafluoride, obtained on excitation with 584 Å monochromatic radiation [113], shows four thresholds of increasing ionisation current (15.35, 16.71, 18.11, and 19.50 eV), three of which correspond to the formation of SF_5^+, probably via the reactions [114]

$$SF_6 + h\nu \rightarrow SF_6^+ + e \ ,$$
$$SF_6^+ \rightarrow SF_5^+ + F \ .$$

The mass spectrum of sulphur hexafluoride was investigated in fair detail [116-128], since studies of this kind make it possible to account for the characteristics of the behaviour of SF_6 as a dielectric. The ability of sulphur hexafluoride to form negative ions on irradiation with low-energy electrons [116] is of great practical interest in connection with its characteristic large electron capture cross-section [32,33,115].

The mechanism of the interaction of sulphur hexafluoride with low-energy electrons (0–2 eV) can be represented schematically by the resonance absorption (capture) of an electron with formation of a metastable ion:

$$SF_6 + e \rightleftarrows (SF_6^-)^* \ , \qquad (1)$$

the ion either dissociates (dissociative capture):

$$(SF_6^-)^* \rightarrow SF_5^- + F \ , \qquad (2)$$
$$SF_5 + F^-$$

or is stabilised by collision with an extraneous molecule:

$$(SF_6^-)^* + A \rightarrow SF_6 + A \ . \qquad (3)$$

There are also data obtained in studies on sulphur hexafluoride by NMR; ^{19}F NMR spectra have been recorded for both gaseous SF_6 and the hexafluoride fixed in the form of clathrate compounds [129-135].

IV. PHYSICOCHEMICAL PROPERTIES

The main physical properties of sulphur hexafluoride are listed in Table 2. Under normal conditions, SF_6 is a colourless gas with a nearly theoretical density. On cooling to −63 °C, it condenses to a colourless solid, which may be fused under pressure. The triple point parameters are $t = -50.8$ °C and $P = 2.3$ atm. [156] The vapour pressure changes from 3.4 to 26.4 atm in the range from −40° to +30 °C. [157] At 94.30 K there is an endothermic transformation of solid SF_6.

The critical parameters of sulphur hexafluoride are as follows: $P_{cr} = 38.328 \pm 0.05$ kgf cm^{-2}, $t_{cr} = 45.560 \pm 0.05$ °C, and $v_{cr} = 198.0 \pm 0.4$ cm^3 $mole^{-1}$ (Makarevich and Sokolova [158]) and agree well with earlier data [36,139].

The temperature variation of the vapour pressure of SF_6 in the range from −30 °C to t_{cr}, derived by Elema [37] from experimental data [36,139,156,159], is

$$\lg P(\text{bars}) = 4.40538 - 8.47739/\theta - 3.72000/\theta^2 + 5.33334/\theta^3,$$

where $\theta = T/100$.

At the same time Mears et al. [160] obtained the following relation between the vapour pressure and temperature in the range 25–130 °C (the temperature in both equations are expressed on the Kelvin scale) using their own data and results quoted in the literature [137,139]:

$$\lg P(\text{bars}) = 4.41780 - 889.185/T - 0.56334 \times 10^{-3}T + 0.120040 \times 10^{-5}T^2.$$

The temperature variation of the density of liquid sulphur hexafluoride can be represented by a five-term equation [160]:

$$d(\text{g cm}^{-3}) = A_0 + \sum_{n=1}^{n=4} A_n(1 - T/318.80)^{n/3},$$

where $A_0 = 0.725$, $A_1 = 1.4721$, $A_2 = -0.282881$, $A_3 = 1.302590$, and $A_4 = -0.628493$. The absolute error in the determination of the density in the range from −41 ° to +42 °C does not exceed 0.1%.

The sublimation pressure of solid SF_6 is described by the equation

$$\lg P(\text{mmHg}) = A - B/T,$$

which is probably valid in the temperature range from 102 to 222 K (Table 3).

Table 2. Physical properties of sulphur hexafluoride.

Property	Value	References
Melting point, °C	−50.8	136
Sublimation temperature, °C	−63.8 (760 mmHg)	136
Critical temperature, °C	45.642, 45.547, 45.55	36, 137–139
Critical pressure, atm	37.193, 37.113, 38.27, 38.15	36, 137–139
Heat of fusion, kcal $mole^{-1}$	1.201, 1.1, 1.39	136, 140, 141
Heat of sublimation, kcal $mole^{-1}$	5.64, 5.57, (−63.8)	136, 141, 142
Density of gas, g $litre^{-1}$ (20 °C)	6.093 (753.5 mmHg)	143
Density of solid, g cm^{-3}	2.683 (−195°), 2.51 (−50°)	136
Density of liquid, g cm^{-3}	1.37 (20°), 1.722 (−20°), 1.787 (−39°), 1.818 (−45°), 1.878 (−50°)	136, 138, 144, 145
Critical density, g cm^{-3}	0.74, 0.73, 0.7517, 0.741	36, 137, 138, 146
Surface tension, dyn cm^{-1}	11.63 (−50°), 8.02 (−20°)	145, 147
Viscosity of gas, 10^4CGS units	1.537 (22.5°), 1.871 (100°)	148
Molecular diameter, Å (from viscosity)	4.77	148
Thermal conductivity (of liquid), 10^5W cm^{-1} deg^{-1}	13.2 (20°), 13.6 (30°), 14.3 (50°)	149
Thermal conductivity (of gas), 10^4W cm^{-1} deg^{-1}	1.3 (20°, 1 atm)	150
Refractive index (of liquid)	1.170 (20°), 1.167 (25°)	151
Dielectric constant (at 27.6 °C), CGS units	1.009191 (178 mmHg) 1.00123 (457 mmHg) 1.00034 (131 mmHg)	152, 153
Dipole moment, CGS units	$3 \cdot 10^{-20}$	154
Velocity of sound, m s^{-1}	146.3 (30°, 750 mmHg)	155
Magnetic susceptibility, CGS units	$(-0.300 \pm 0.003) \cdot 10^{-6}$	142

Solubility of Sulphur Hexafluoride

The behaviour of SF_6 in polar and non-polar solvents (Table 4) is of undoubted practical[164-167] and theoretical[168-170] interest. The solubility of sulphur hexafluoride in water (5.5×10^{-3} cm^3/cm^3 H_2O), determined for the first time by Friedman[171], is much lower than the solubilities of gases as helium (9×10^{-3}), molecular nitrogen (16×10^{-3}), xenon (118×10^{-3}), or argon (34×10^{-3}). The experimental entropy of solution (−50 e.u.) proved to be higher by more than 10 e.u. than the values calculated empirically[177-179]. The enthalpy of solution is also more negative than the enthalpy of condensation of SF_6, which is −4 kcal $mole^{-1}$.

Table 3. The constants A and B in the equation $\lg P = A - B/T$ for the sublimation pressure of sulphur hexafluoride.

Temperature range, K	A	B	References
175—222.5	8.711	1222	136
201—222.5	8.7648	1231.3	161
200.7—222.5	8.736	1224.8	162
102—143	8.9555	1265	163

Table 4. The solubilities of sulphur hexafluoride in various solvents (t = 25°C, P = 1 atm).

Solvent	10^4 × mole fraction	References	Solvent	10^4 × mole fraction	References
H_2O	0.05*	173	C_7F_{16}	224.4	175
HF	1.3**	174	CCl_4	65.54	174
C_6F_6	26.4	174	$C_2Cl_3F_3$	278.6	174
C_6H_{12}	53.91	174	CS_2	9.245	175
n-C_7H_{16}	100.55	174	$(C_4F_9)_3N$	731	176
i-C_8H_{18}	153.5	174	$N_2H_3CH_3$	2.11	167
$C_6H_5CH_3$	33.95	174	N_2O_4	93.46	167
$C_6H_{11}CH_3$	70.15	174	CH_3NO_2	10.0*	171

*Recalculated from data of Ashton et al.[172]
**Recalculated from data of Gillespie and Humphreys[173].

It is noteworthy that the estimates of the thermodynamic properties of solution when the solubility of the gas is so low may not be adequately reliable. The use of better apparatus (accuracy to within a mole fraction of 10^{-6}) made it possible to obtain an expression for the temperature variation of the solubility of SF_6 in water, in the range 0–50°C:[172]

$$\lg X_2 = 6648.32/T + 45.2067 \lg T - 139.5793,$$

where X_2 is the mole fraction of SF_6 in water and T the temperature in K.

The heat and entropy of solution of sulphur hexafluoride can be determined from the relations.

$$\Delta H_2^\circ/R = \partial \ln X_2/\partial(1/T) = -2.303 \times 6648.32 + 45.2067\,T,$$

where the entropy of solution refers to the transfer of 1 mole of gas to a hypothetical solution of unit mole fraction. The enthalpy and entropy of solution of SF_6 in water calculated by this formula are respectively −4.9 kcal $mole^{-1}$ and −41 cal $mole^{-1}$ deg^{-1} [at 25°C].

The Formation of Clathrate Compounds

It is interesting to note that, despite the low solubility of sulphur hexafluoride in water and other solvents, the existence of two clathrate compounds of SF_6 has been established: the gas hydrate $SF_6.17H_2O$ and the clathrate derivative formed by Dianin's compound with sulphur hexafluoride ($6C_8H_{20}O_2.2SF_6$).[180-184]

The gas hydrate can be obtained by slowly forcing SF_6 into water until the gas pressure reaches 5–6 atm. White crystals resembling snow are formed at 0°C. It was established on the basis of the P–T phase diagram in the temperature range between −9° and 15°C that the gas hydrate of sulphur hexafluoride contains 17.02 moles of water per mole of sulphur hexafluoride at 0°C.[181] The vapour pressure at this temperature is 0.8 atm. The heats of formation of the hydrate from liquid water and ice are respectively −29.57 and 5.140 kcal $mole^{-1}$. The temperature and pressure corresponding to the coexistence of four phases (the SF_6 hydrate–liquid enriched in water–liquid enriched in SF_6–vapour) are 14°C and 20 atm.

The clathrate derivative formed by Dianin's compound[182,183] with sulphur hexafluoride can be obtained by keeping the ethanol modification of this compound, dissolved in decanol, at a 20–25 atm pressure of gaseous SF_6 and 130–140°C for 4–5 days. This results in the formation of a solid clathrate derivative whose composition is close to $6C_{18}H_{20}O_2.1.79SF_6$.[184] The product contains up to 13% SF_6, i.e. a little less than 2 moles (14.7%), probably owing to the limited solubility of sulphur hexafluoride in decanol. The melting point of the clathrate compound $6C_{18}H_{20}O_2.1.79SF_6$ is 163–165°C and its density is 1.3 g cm^{-3}.

It is quite evident that the capacity for the formation of clathrate compounds is not unusual for sulphur hexafluoride and the small number of examples known at present is due merely to the current state of research in this field. There is no doubt about the great promise and theoretical and practical value of the latter.

Thermochemical Properties

The heat of formation of sulphur hexafluoride under standard conditions was determined from calorimetric measurements of the heat of combustion of sulphur in fluorine. Such measurements were made for the first time by Yost and Claassen[141], who found ΔH_{298}° = −262 kcal $mole^{-1}$. A later study of a similar kind by Gross[185] yielded −288.5 ± 0.7 kcal $mole^{-1}$ as the heat of formation of SF_6 under standard conditions and, finally, according to O'Hare et al.[186], ΔH_{298}° = −291.7 ± 0.2 kcal $mole^{-1}$. The last value is probably the most accurate, which was confirmed by redeterminations using fluorine with a lower oxygen content[185].

The heat capacity of sulphur hexafluoride was determined experimentally by Eucken and Schröder[140] up to 13 K. These results were used by Kelley and King[187] to calculate the standard entropy of formation of SF_6, which proved to be 70.3 ± 0.7 cal $mole^{-1}$ deg^{-1}, in agreement with statistical calculations of this quantity: 69.5 to 70.7 cal $mole^{-1}$ deg^{-1}.[186,188-191]. The small differences between the entropies calculated by the statistical method are largely due to the differences between the molecular constants and particularly the S–F bond lengths employed.

Thermal Stability

The thermal dissociation of sulphur hexafluoride results in a gaseous mixture containing mainly the following components: S, F, e, SF_6, SF_4, SF_3, SF_2, SF, S_2, F_2, S^{2+}, F^+, F^-, and S^-.[192-195] Calculation of the mixture composition in the temperature range 1000–20 000 K at pressures of 1–20 atm in the dissociation range showed that

at 1000 K the mole fraction of atomic fluorine and sulphur tetrafluoride is 6×10^{-6} and that of molecular fluorine is 1×10^{-6}. Up to 1400 K ($P = 1-10$ atm), the mole fraction of SF_6 is still close to unity (0.992). Rapid dissociation begins at 2000 K with the appearance of new species: S, SF_2, SF, and S_2. At 3000 K SF_6 no longer exists and the decomposition products begin to be enriched in the ions S^+, F^+, F^-, and S^-. SF_4 disappears at 5000 K and the remaining molecules vanish at 7500 K, the plasma consisting of electrons, sulphur, and fluorine in atomic and ionised states [195].

V. CHEMICAL PROPERTIES

The chemical activity (reactivity of a particular compound is determined by the rate of reaction between the latter and another substance, provided of course that the process itself is thermodynamically feasible. In order to compare the reactivities of various compounds in relation to the same substance, the reaction rates compared must refer to the same stage, common to the processes under consideration occurring under comparable conditions. The isolation of the rate determining stage of the reaction and observation of the latter involve considerable difficulties, which increase on passing from homogeneous to heterogeneous systems. Therefore in practise one usually employs a systematic empirical procedure frequently based on qualitative observations. Naturally, such a procedure may be unreliable. Thus, recent studies of the chemical properties of molybdenum and tungsten hexafluorides [10,11] showed that both compounds are appreciably inert, in contrast to earlier investigations in which MoF_6 and WF_6 were regarded as vigorous fluorinating agents[29,196]. The difficulties of the empirical approach faced investigators with the necessity to establish some, at least qualitative, criteria for the prediction of the potentially possible changes in the chemical systems of the hexafluorides of several elements, since such systems are of some practical interest. One of these criteria is the thermal stability of the hexafluorides.

A comparative estimate of the thermal stabilities was made most completely and in greatest detail, using various physicochemical characteristics (the force constants of EF_6, the E–F bond energies, and the equilibrium constants for the dissociation reactions), by Galkin and Tumanov[2]. Table 5 presents the thermal stability series of the hexafluorides established by the authors on the assumption that the thermal stability is related to various physicochemical characteristics of the SF_6 molecule.

Analysis of the results led the authors to the conclusion[2] that the most objective criterion of the thermal stability of hexafluorides as a characteristic of their reactivity is apparently the thermodynamic stability constant (the reciprocal of the equilibrium constant for the dissociation reaction), characterising the partial dissociation of the hexafluorides to the corresponding tetrafluorides. The thermal stability estimated from the average E–F bond energy in EF_6 agrees fully with the thermodynamic estimate with the exception of ReF_6. The valence force constants and the interatomic distances are of the doubtful value, according to the authors, as characteristics of the chemical properties of hexafluorides.

† It was assumed that an increase in the thermal stability of the molecule entails a decrease of its reactivity [197].

Returning now to sulphur hexafluoride, it can be shown by estimating its reactivity from the thermodynamic stability constant that it is a fairly reactive substance capable of converting into the highest fluorides at any rate compounds of metals such as molybdenum, tungsten, or uranium. Indeed the conversion of UO_2 into UF_6 with the aid of sulphur hexafluoride was achieved recently [52].

On the other hand, the list of substances in relation to which sulphur hexafluoride is fairly reactive can be greatly extended if one assumes the possibility of another reaction pathway, based, for example, on the high electron affinity of SF_6. We may recall that sodium dissolved in the dimethyl ether of diphenylethylene glycol reduces sulphur hexafluoride even at room temperature and the reaction is apparently based on electron transfer from a diphenyl radical-ion to the SF_6 molecule with formation of the unstable radical-anion SF_6^-. [84]

Table 5. Variation of the thermal stabilities of hexafluorides with certain physicochemical characteristics of the molecules.

Physicochemical characteristic of the molecule	Variation of thermal stabilities with increase of the physicochemical characteristic of the molecule
Bond energy D_0^0	$UF_6>WF_6>NpF_6>MoF_6>PuF_6>ReF_6>TcF_6>OsF_6>>TeF_6>SF_6>SeF_6>IrF_6$
Thermodynamic stability constant: $MF_6 \rightarrow M(gas) + 6F(gas)$	$UF_6>WF_6>NpF_6>MoF_6>PuF_6>TcF_6>ReF_6>OsF_6>>TeF_6>SF_6>SeF_6>IrF_6$
Thermodynamic stability constant: $MF_6 \rightarrow MF_4(gas) + 2F(gas)$	$WF_6>MoF_6>UF_6>SF_6>NpF_6>PuF_6$

The above considerations should be used as the starting point in the search for ways of increasing the reactivity of sulphur hexafluoride in order to use it as a fluorinating agent. This is quite feasible, since the inertness of sulphur hexafluoride can be successfully overcome by various process activation procedures, including ordinary heating.

Reactions in an Electric Discharge

The lower sulphur fluorides (SF_2 and S_2F_2), whose reactivity is much higher than that of the initial sulphur hexafluoride, are formed under the conditions of an electric discharge [198-201].

The effect of a high-frequency electric discharge was used for preparative purposes in reactions of sulphur hexafluoride with chlorine and oxygen [202]. In the first case the process is accompanied by the formation of SF_5Cl, probably in accordance with the overall equation

$$SF_6 + Cl_2 \rightarrow SF_5Cl + ClF \quad .$$

The yield of SF_5Cl is 1.97×10^{-3} mole h^{-1}. Chlorine monofluoride (ClF) was not identified, evidently owing to its reaction with glass.

The reaction between SF_6 and O_2 (in proportions of 1.32 : 1) leads to the formation of SOF_4, the approximate yield of which is 0.11×10^{-2} mole h^{-1} (degree of conversion 18%) at a gas flow rate of 0.61×10^{-2} mole h^{-1}. The mechanisms of the two reactions could not be determined owing to the abundance of the SF_6 dissociation and ionisation products formed under the influence of the electric discharge.

Reaction Accompanying the Explosion of Metallic Wires in an Atmosphere of SF_6

Studies on the pyrolysis of hydrocarbons under the conditions of exploding wires using sulphur hexafluoride as the inert diluent established that the latter reacts with the exploding metals even at relatively low levels of the supplied energy [56,203,204]. This results in the formation of either the corresponding metal fluoride and sulphur tetrafluoride:

$$2/n\,M + SF_6 = 2/n\,MF_n + SF_4 \qquad (4)$$

or of the metal fluoride and elemental sulphur:

$$6/n\,M + SF_6 = 6/n\,MF_n + S \ , \qquad (5)$$

where n is an index corresponding to the highest degree of oxidation of the metal.

The particular reaction pathway depends on the molar ratio SF_6 : M. For example, the reaction with tungsten for the ratio SF_6 : W = 3.0 takes place in accordance with Eqn. (4). The fraction of WF_6 obtained by reaction (5) increases to 42% when the molar ratio of the components is 1.8. The yield of MoF_6 in reaction (5) involving molybdenum varies from 12 to 52% when the molar ratio SF_6 : Mo is reduced from 2.0 to 1.6 respectively.

The explosion of rhenium in an atmosphere of SF_6 leads to the formation of the volatile rhenium hexafluoride and heptafluoride. By selecting appropriate conditions, it is possible to obtain rhenium heptafluoride in which the ReF_6 content is minimal. Moreover the hitherto unknown involatile rhenium fluoride ReF_3, which cannot be obtained by direct synthesis from the elements, was formed in this reaction.

Thus sulphur hexafluoride becomes a very effective fluorinating agent under the conditions where a metal is exploded electrically. The processes investigated lead to the possibility of new syntheses of both SF_4 and specific metal fluorides without the use of elemental fluorine. It is interesting to note that the yield of reaction products is independent of the stoichiometry of the initial components, while the composition does depend on the latter. This makes it possible to regulate the purification of the volatile fluorides formed and it can serve as a basis for the synthesis of hitherto unknown inorganic fluorides.

The explosion of extremely small amounts of platinum or copper can initiate the above reaction between SF_6 and O_2, but the yield is lower [205,206].

The high kinetic barrier to the reaction between SF_6 and O_2 is probably due to the ability of fluorine to repel the electronegative oxygen [206]. In fact the rate of reaction can be increased appreciably in the presence of various gaseous additives (promoting agents), for example H_2, Cl_2, Br_2, and CH_4, the effectiveness of the promoting agent being inversely proportional to its electronegativity:

$$CH_4 > H_2 > Br_2 > Cl_2 \ .$$

Ion–Molecule Reactions

The SF_6 molecule belongs to the class of halogen-containing molecules, which are of considerable theoretical interest in connection with their characteristic large electron capture cross-sections. The radical-anion SF_6^- (or SF_5^-) formed on interaction with electrons is very reactive with respect to a series of fluorine-containing molecules: PF_3 and PF_5, [207] SiF_4 and BF_3, [208] and POF_3 and PSF_3. [209] Thus, when a mixture of two fluorides (SF_6 and AF_n) is introduced into an ionisation chamber and bombarded with thermal electrons (0–0.2 eV), the formation of AF_{n+1}^- anions may be observed in the mass spectrum:

$$AF_n + SF_6^- (SF_5^-) \rightarrow AF_{n+1}^- + SF_5 (SF_4) \ .$$

These cannot be formed independently under the given conditions (BF_4^- and SiF_5^- are observed in the mass spectrum only for energies in excess of 10 eV). [210,211]

Reactions on γ-Radiolysis

The high electron affinity of sulphur hexafluoride made it possible to use the latter as a specific electron acceptor in γ-radiolysis of substances [212–217], influencing in some way the composition of the final reaction products. The γ-radiolysis of water in the presence of SF_6, which was investigated recently, is accompanied by a high yield of F^-, which is formed only by the reaction between SF_6 and $\bar{e}$.aq. The reaction mechanism quoted above is consistent with the experimental data [212]:

$$SF_6 + \bar{e}aq \rightarrow (SF_6^{\cdot})^- \rightarrow SF_5^{\cdot} + F^- \ , \qquad (6)$$

$$SF_5^{\cdot} + 2H_2O \rightarrow OH^{\cdot} + H_3O + SF_4 + F^- \ , \qquad (7)$$

$$SF_4 + 9H_2O \rightarrow SO_3^{2-} + 6H_3O + 4F^- \ , \qquad (8)$$

$$SO_3^{2-} + OH;\ SF_6;\ H_2O_2 \rightarrow SO_4^{2-} \ . \qquad (9)$$

The Photochemical Effect of Infrared Radiation

Basov et al. [218], who studied the effect of infrared radiation from a CO_2 laser ($\lambda = 10.6\ \mu m$) on reactive gaseous systems, established that at certain intensities the vibrationally excited molecules react chemically. Thus irradiation of the N_2F_4–NO–$C_2F_4(C_2F_6)$ system results in a bright greenish-yellow flash, accompanying the process, and the starting materials react completely. It is noteworthy that, on normal heating of the system, the process is possible only at temperatures above 1500 K.

Irradiation of the SF_6–NO mixture also leads to an instantaneous reaction accompanied by a flash. SOF_2 is formed as one of the products. According to the authors, the mixture temperature does not then exceed 700°C, while the thermally activated mixture remains unreactive up to 1000°C. However, one should note that the conversion of SF_6 and NO is not complete. Pankratov [219] noted that this is due to the fact that the appearance of chemical reactivity may be caused by the excitation of stretching vibrations alone, while the radiation generated by the laser corresponds to the range of SF_6 deformation vibrations.

The results demonstrate the possibility of specific reactions, since the reaction of mixtures of starting materials under the influence of infrared radiation can be different from that at elevated temperatures when heated in the usual way. This factor is extremely important, since it leads to a method of synthesising new compounds involving extensive application of lasers in chemistry.

The Reaction on Heating

It is noteworthy that the simple and generally adopted method of accelerating reactions such as ordinary heating has for a long time been ignored by investigators, evidently in view of the negative results of the early studies mentioned above.

Despite Moissan's view that sodium is not acted upon by sulphur hexafluoride up to the boiling point of the metal (880°C), it was established in 1953 [220] that the reaction occurs even at 247°C ($K = 2.23 \times 10^{13}$ cm^3 mole^{-1} s^{-1}). At 500°C the reaction is accompanied by chemiluminescence, the most likely explanation of which is that one of the five stages is exothermic with liberation of sufficient energy to excite the sodium D line:

$$SF_6 + n\,Na \rightarrow SF_{6-n} + n\,NaF \quad .$$

At relatively low temperatures (180–200°C) sulphur hexafluoride fluorinates aluminium trichloride with an AlF_3 yield of the order of 15% and at 250°C it reacts with SO_3, forming sulphuryl fluoride in approximately 20% yield [221]:

$$2SO_3 + SF_6 = 3SO_2F_2 \quad .$$

Technological reports dealing with the regeneration of waste from nuclear fuel by its fluorination with sulphur hexafluoride were published recently [52,53]. For example, the fluorination of UO_2 in corundum reactors at 750 to 900°C with an $SF_6 : O_2 = 1 : 1$ mixture is accompanied by the formation of UF_6. The authors believe that the process proceeds in accordance with the following general reaction mechanism [52]:

$$UO_2 + SF_6 = UF_6 + SO_2 \quad .$$

The use of high temperatures (1000°C) made it possible to obtain under laboratory conditions comparatively pure protactinium pentafluoride by fluorinating protactinium pentoxide with sulphur hexafluoride [53]:

$$3Pa_2O_5 + 5SF_6 = 6PaF_5 + 5SO_2 + 2.5O_2 \quad .$$

Moreover, the same authors' thermodynamic calculation has shown that the high-temperature fluorination of PuO_2 can yield PuF_4 via the reaction

$$PuO_2 + SF_6 = PuF_4 + SO_2F_2$$

or

$$^3/_2PuO_2 + SF_6 = ^3/_2PuF_4 + SO_2 + ^1/_2O_2 \quad .$$

However, these calculations have not so far been confirmed experimentally.

Naturally the problem of the reactivity or inertness of sulphur hexafluoride can be solved in the light of the above facts only by a comprehensive investigation of its reactivity in relation to a number of elements and their compounds. Such a study was undertaken by the authors of the present review [60–67] and showed that the widely held view that SF_6 is chemically inert is extremely arbitrary and that the example quoted constitute exceptions rather than the rule.

It was established by differential thermal analysis (DTA) that the vast majority of the metals investigated (Table 6) react at a high rate in the range 500–600°C. [61]

The reactions with titanium and the lanthanides proceed particularly vigorously with inflamation. The rate of reaction with boron and silicon is not so high as with titanium or lanthanum, apparently because of the kinetic characteristics of the process, since, on raising the SF_6 flow rate, the reaction is so vigorous in this case too that the mixture becomes incandescent. In many instances the occurrence of the reaction can be detected from the change in the weight of the reaction product relative to that of the starting material.

Our thermodynamic assessment of the most probable processes occurring in the SF_6–M systems led to the following findings:

$$(1/n)M(solid) + \tfrac{1}{2}SF_6(gas) = (1/n)MF_n(solid) + \tfrac{1}{2}SF_4(gas), \qquad (I)$$

$$\Delta G_I^\circ = \Delta H^\circ_{MF_n} - T(S^\circ_{MF_n} - S^\circ_M) + 52250 \text{ cal equiv.}^{-1};$$

$$\tfrac{4}{3}nM(solid) + \tfrac{1}{6}SF_6(gas) = (1/n)MF_n(solid) + \tfrac{1}{6}nM_2S_n(gas), \qquad (II)$$

$$\Delta G_{II}^\circ = \Delta H^\circ_{MF_n} + \tfrac{1}{3}\Delta H^\circ_{M_2S_n} + \tfrac{1}{3}(4S^\circ_M - 3S^\circ_{MF_n} - S^\circ_{M_2S_n} + 34.9) + 48100 \text{ cal equiv.}^{-1};$$

$$(1/n)M(solid) + \tfrac{1}{6}SF_6(gas) = (1/n)MF_n(solid) + \tfrac{1}{12}S_2(gas), \qquad (III)$$

where $\Delta H^\circ_{MF_n}$ and $\Delta H^\circ_{M_2Sn}$ are the standard enthalpies of formation of the fluoride and sulphide respectively (in cal equiv.$^{-1}$), $S^\circ_{MF_n}$ and $S^\circ_{M_2S_n}$ are the standard entropies of formation of the fluoride and sulphide respectively (in cal equiv.$^{-1}$ deg^{-1}), and S°_M is the standard entropy of the metal (in cal equiv.$^{-1}$ deg^{-1}).

Table 6. Conditions in the reaction of sulphur hexafluoride with metals and oxides.

Metal or oxide	T, °C	ΔP, %	Metal or oxide	T, °C	ΔP, %	Metal or oxide	T, °C	ΔP, %
K	400	—	Sb	none	—	Tb_4O_7	637	—
Cu	none	+30	W	648	—88	Dy_2O_3	645	14.5
Mg	none	+9.5	Re	none	—	Ho_2O_3	642	14.6
Ca	470	—	MgO	795	+61	Er_2O_3	597	+11.7
Zn	613	+33	CaO	727	+23.1	Tm_2O_3	670	+12.5
Cd	530	—	SrO	628	+12.7	Yb_2O_3	700	+14
B	680	—	BaO	480	+13.4	Lu_2O_3	590	+12
Al	560	—	B_2O_3	none	—	TiO_2	none	+13.5
Ga	690	—	Al_2O_3	530	+24.5	Cr_2O_3	none	+14.5
In	480	—	Ga_2O_3	none	+12.3	WO_3	none	—
La	450	—	In_2O_3	none	+20.6	MnO	none	—
Pr	460	—	Sc_2O_3	none	+28.7	CuO+KF	526	+19
[illegible]	550	—	Y_2O_3	657	+36.4	MgO+KF	474	+7.9
Tm	550	—	La_2O_3	714	+5	CaO+CsF	563	+7.8
Yb	500	—	Ge_2O_3	450	—	SrO+RbF	none	+16
C	none	—8.4	Pr_6O_{11}	584	+13.2	ZnO+KF	none	+6
Si	662	—5	Nd_2O_3	647	+15.4	SnO+KF	332	+20
Sn	none	—	Sm_2O_3	670	+8	TiO_2+NaF	none	—48
Ti	494	—84.6	Eu_2O_3	560	+18.7	VO_2+KF	429	—
Zr	560	—	Gd_2O_3	594	+12.6	Ni_2O_3+KF	none	+23

Note. 1) "none" implies that a thermal effect was not recorded on the thermograms; 2) ΔP is the relative change in weight (wt.%); 3) implies that an increase in weight was not determined.

It can be easily shown that under standard conditions $\Delta G^\circ_{II} < \Delta G^\circ_I < \Delta G^\circ_{III}$, but at high temperatures this relation can change. By solving the inequality $\Delta G^\circ_I - \Delta G^\circ_{II} < 0$ for T, we find that $\Delta G^\circ_I < \Delta G^\circ_{II} < \Delta G^\circ_{III}$ when $T \geq (12450 - \Delta H_{M_2S_n})/S^\circ_M - S^\circ_{M_2S_n} + 34.9)$, i.e. reaction (II), accompanied by the formation of the metal sulphide and fluoride, is thermodynamically most favoured when $T' < T$ and reaction (I), involving the formation of the metal fluoride only, is most likely at $T'' > T$.

A test of the thermodynamic calculations for the metal–SF_6 systems led to their confirmation in a detailed experimental study of the conditions and the nature of the interaction of sulphur hexafluoride with zinc and cadmium [62].

Both metals react with SF_6 after their fusion. X-Ray diffraction established that the reactions of zinc and cadmium with SF_6 involve the formation of the metal fluorides and sulphides.

The products of the reaction between cadmium and SF_6 were separated in water using the different solubilities of CdS and CdF_2. Chemical analysis established that the solute is CdF_2 and that the solid in equilibrium with the solution is CdS. The molar ratio of the two phases is close to $CdF_2 : CdS = 3 : 1$, which makes it possible to formulate the process as follows:

$$4Cd + SF_6 = 3CdF_2 + CdS \quad .$$

As for cadmium, the reaction between zinc and SF_6 is also accompanied by the formation of zinc fluoride and sulphide in the molar proportions $ZnF_2 : ZnS = 3 : 1$. As mentioned above, when the temperature is raised, reaction (I) with the metal becomes thermodynamically favoured. Using inequality (10), it can be shown that the required temperature is above 650°C for cadmium and above 750°C for zinc. Indeed the fluorination of cadmium at this temperature leads to the formation of CdF_2 alone; the reaction with zinc is also accompanied by an increase in the mole fraction of the fluoride up to the formation of pure ZnF_2.

Thus our experimental data in no way confirm a marked chemical inertness of sulphur hexafluoride, showing in fact that, even on moderate heating, SF_6 becomes an active fluorinating agent capable of "supplying" its fluorine to reactions involving the fluorination of both elements and compounds. However, the reaction with oxides takes place at higher temperatures (Table 6). The only solid product is the difluoride of the corresponding metal.

Thermodynamic analysis (under standard conditions) of the reactions between sulphur hexafluoride and metals of one of the types

$$^1/_2n\,M_2O_n + {}^1/_4SF_6 = 1/n\,MF_n + {}^1/_4SO_2F_2 \quad , \qquad (10)$$

$$^1/_2n\,M_2O_n + {}^1/_6SF_6 = 1/n\,MF_n + {}^1/_6SO_3 \quad , \qquad (11)$$

$$^1/_2n\,M_2O_n + {}^1/_4SF_6 = 1/n\,MF_n + {}^1/_4SOF_2 + {}^1/_8O_2 \quad , \qquad (12)$$

$$^1/_2n\,M_2O_n + {}^1/_6SF_6 = 1/n\,MF_n + {}^1/_6SO_2 + {}^1/_{12}O_2 \quad , \qquad (13)$$

$$^1/_2n\,M_2O_n + {}^1/_2SF_6 = 1/n\,MF_n + {}^1/_2SOF_4 \quad . \qquad (14)$$

shows that at 550°C all the reactions [except reaction (14)] are already thermodynamically feasible. A mass-spectrometric study of the composition of the gas phase showed[63] that the reaction products are sulphur dioxide and sulphuryl fluoride. The absence of sulphur trioxide can be readily accounted for, on the one hand, by its dissociation at the given temperatures and, on the other, by the possibility of its interaction with SF_6. Nor can one rule out the possibility that the sulphur oxide fluorides formed can themselves behave as fluorinating agents. The latter is of fundamental importance from the standpoint of the maximum utilisation of the fluorine contained in the initial sulphur hexafluoride. One may also note that the thermodynamic calculations are fully consistent with the experimental data, which showed the absence of sulphur oxide tetrafluoride from the gaseous reaction products, since ΔG°_{290} for reaction (14) is positive over the entire temperature range.

A number of investigators[222-225] have recently attempted to establish a quantitative relation between thermodynamic and kinetic process characteristics for reactions of the same type. Thus a study of reactions between the oxide of a Group IVA element and chlorine demonstrated the existence of an approximately linear relation between the free energy of reaction ΔG° and the temperature of the onset of reaction T_i, determined by the DTA method. If it is assumed that such correlations for reactions of the same type [reactions (10)–(13)] do occur, then T_i for any of the above reactions will be determined mainly by the difference $\Delta H^\circ_{MF_n} - \Delta H^\circ_{M_2O_n}$ kcal equiv.$^{-1}$, decreasing as the difference diminishes. It is noteworthy that T_i for reactions of the same type, whose rates do not differ appreciably, can serve as a qualitative measure of the reactivity of a particular component.

On the basis of the above hypothesis, T_i presumably decreases (and the reactivity of SF_6 increases) in the vertical series of the oxides of Group IA elements: $Li_2O > Na_2O > Cs_2O > K_2O = Rb_2O$, since $\Delta H^\circ_{MF_n} - \Delta H^\circ_{M_2O_n}$ varies in the sequence $Rb_2O = K_2O > Cs_2O > Na_2O > Li_2O$; for the oxides of Group IIA elements, we have $BeO > MgO > CaO > SrO > BaO$, since $\Delta H^\circ_{MF_n} - \Delta H^\circ_{M_2O_n}$ varies in the sequence $BaO > SrO > CaO > MgO > BeO$; finally for the oxides of Group IIIA elements we have $Al_2O_3 > In_2O_3 > Ga_2O_3 > Tl_2O_3$, since $\Delta H^\circ_{MF_n} - \Delta H^\circ_{M_2O_n}$ varies in the sequence $Tl_2O_3 > Ga_2O_3 > In_2O_3 > Al_2O_3$.

Table 6 shows that a similar correspondence is in fact observed for the oxides of Group IIA elements (MgO, CaO, SrO, and BaO) and Group IIIA elements (Al_2O_3, Ga_2O_3, and In_2O_3), despite the fact that T_i for In_2O_3 (610°C) and Ga_2O_3 (680°C) were determined by differential thermogravimetric analysis. All the lanthanide oxides react in the temperature range 450–700°C like the oxides of alkaline earth metals but even more vigorously (Table 6). Consideration of data for the oxides La_2O_3, Nd_2O_3, and Pr_6O_{11} shows that, according to the results of chemical and X-ray diffraction analyses, they react with sulphur hexafluoride, forming the corresponding metal trifluorides.

It is noteworthy that SF_6 is an extremely vigorous fluorinating agent on heating in the synthesis of not only binary fluorides but also complex fluorides. We showed this in a study of the reaction of sulphur hexafluoride with alkaline earth metal oxides in the presence of an alkali metal fluoride[64]. Alkaline earth metal complexes of the type M^IMF_3 synthesised in the solid phase are formed only at fairly high temperatures above 1000°C,[226,227] which naturally gives rise to certain difficulties both in the synthesis and in the subsequent purification of the products. On the other hand, in the fluorination of a mixture of an alkaline earth metal oxide and an alkali metal fluoride in specific stoichiometric proportions the corresponding complexes are formed at lower temperatures. For example, $KMgF_3$ was obtained under these conditions at 660°C, while the solid-phase synthesis requires the use of temperatures above 1000°C. The syntheses of the corresponding fluoro-complexes of alkaline earth metals were achieved under similar conditions: K_2MgF_4, $CsMgF_3$, $CsGaF_3$, $CsSrF_3$, and $BaLiF_3$. It was established by the DTA method that the temperature of the onset of reaction between SF_6, MO, and MF does not exceed 500°C in all cases. Under these conditions and up to 900°C, the MF_2–MF mixture does not undergo any changes associated with the formation of complex fluorides. The latter can be obtained in the MF_2–MF system only at temperatures not less than 1100–1200°C.[226,227]

Thus the above results show that sulphur hexafluoride is an extremely active fluorinating agent and can be used successfully in the synthesis of anhydrous binary and complex fluorides.

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Presumably further advances in the application of sulphur hexafluoride (one of the most widely used hexafluorides) will be achieved primarily in connection with studies on its chemical properties, since the level of present research on the physical and physicochemical properties meets practical requirements adequately.

In this respect the most interesting and in practise most important results may be expected in studies on reactions where SF_6 behaves as a fluorinating agent. The practical interest in reactions of this kind is due to the high fluorine content in sulphur hexafluoride (78%), its inertness and non-toxicity under the usual conditions, and also the possibility of its activation by various procedures, ranging from the effect of electromagnetic radiation to ordinary heating. The data obtained by the present authors for the synthesis of both simple and complex inorganic fluorides involving sulphur hexafluoride suggest that SF_6 can be regarded as a new and very promising fluorinating agent, the possibilities of which have been by no means fully explored. It is quite evident that the requirements of both scientific research and industry involve extensive employment of increasing numbers of new fluorinating agents. Traditional fluorine, fluorine halides, and hydrogen fluorides can be in many cases replaced successfully by noble gas fluorides[228,229], alkali metal fluoride halides[230] and hydrogen fluorides[230-233], nitrogen[234] and phosphorus[235] fluorides, and the highest fluorides of certain metals[236]. There is no doubt that one is fully justified in including sulphur hexafluoride in the above by no means exhaustive list of the possible and promising fluorinating agents, this being confirmed by the advances in the chemistry of this compound.

The reactions of SF_6 with various gaseous compounds initiated by laser radiation are extremely interesting from the standpoint of the synthesis of new fluorine-containing compounds.

The study of the solubility of sulphur hexafluoride in water and other solvents is extremely fruitful in relation to further investigations of the nature of non-electrolytes and is of interest in connection with the possible synthesis of various derivatives of sulphur hexafluoride in non-aqueous media.

It is noteworthy that, although the method of synthesis of sulphur hexafluoride from the elements is fairly simple, it requires the use of expensive fluorine and of expensive apparatus in view of the corrosive nature of fluorine. The advances in recent years nevertheless give rise to the hope that it will be possible to introduce methods for the synthesis of sulphur hexafluoride without the direct use of fluorine, for example by the electrolysis of sulphur-containing compounds in liquid hydrogen fluoride.

The development of studies on the chemistry of this compound will undoubtedly entail the necessity for the development of the analytical chemistry of SF_6 and it appears likely that gas or gas–liquid chromatography will prove to be most useful in this field too.

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Activation of Molecular Oxygen on Interaction with Transition Metal Complexes

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The present state of research and ideas in the field of the activation of molecular oxygen by transition metal complexes and matrix systems is described.
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I. INTRODUCTION

One way of increasing the reactivity of oxygen is its "chemical" activation, in particular its fixation on transition metal complexes. It is suggested that, owing to the many possible valences in the complexes, the activated molecule can not only react under mild conditions but also exhibits a definite selectivity in relation to the substrate.

The formation of complexes by molecular oxygen can occur in many heterogeneous catalytic oxidation processes[1], in the autoxidation of complexes[2], and also in biochemical processes. The mechanism of action and the functions of oxygen carriers in such processes are usually elucidated with the aid of homogeneous models[3-5]. Transition metal complexes, which are capable of binding molecular oxygen, are normally employed as model systems.

Two approaches to the study of the mechanism of the activation of oxygen via its coordination have been devised.

In the first, analytical approach the aim is to select a theoretical quantum-chemical model which can describe satisfactorily the binding of molecular oxygen and can predict the possible reactivity of coordinated oxygen. This approach presupposes the existence of a definite relation between the geometry of the dioxygen complex, the nature of the binding of oxygen, and a definite type of reactivity of the coordinated oxygen molecule.

The second approach involves the creation of synthetic models of heterogeneous and biochemical systems in which molecular oxygen is fixed. The approach is based on matrix effects, i.e. the aim is to simulate the conditions for the fixation of oxygen in systems with polymeric structural elements.

A combination of these two approaches in the study of the mechanism of the activation of molecular oxygen is probably the most fruitful.

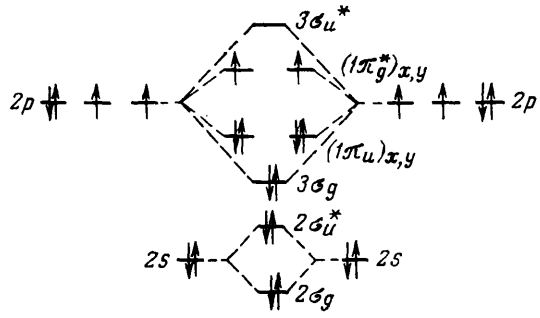
A number of reviews on this problem have been published in which the structure, binding, and reactivity of dioxygen complexes are discussed fairly extensively[6-11] and the general characteristics of the binding of oxygen are analysed[12,13].

Analogous processes have been dealt with in Soviet scientific literature: the activation of small molecules and new trends in the development of the chemistry of coordination compounds[14] and homogeneous catalytic oxidation of hydrocarbons[15]. However, one should note that the problem of activated binding and also the matrix principle of the fixation and activation of the oxygen molecule have not so far been adequately described.

In the present review an attempt is made to survey the latest results of studies of this kind.

II. THE STRUCTURE OF THE OXYGEN MOLECULE AND ITS ACTIVE FORMS

The structure of the oxygen molecule can be conveniently treated within the framework of molecular orbital method[16]. The two least strongly bound electrons are placed in doubly degenerate antibonding π orbitals and, according to the Hund rule, have parallel spins, i.e. the molecule has a triplet ground state $^3\Sigma_g$ (Fig. 1).



The bond between the atoms is due to the interaction of $2p$ electrons and consists of one two-electron σ bond $(3\sigma_g)^2$ and two three-electron π bonds $(1\pi_u)^2(1\pi_g^*)^1$. Each three-electron bond constitutes a combination of a pair of

bonding electrons and one antibonding electron in the same interaction plane. The bond order, defined as half the difference between the numbers of bonding and antibonding electrons, is two.

In chemical reactions of oxygen it is necessary to take into account the first excited state of the molecule $^1\Delta$(singlet) in which both π_g^* electrons occupy the same orbital and have antiparallel spins. The formal bond order is the same as in the ground state but the electron density is distributed less uniformly, since one π-interaction plane contains two electrons and the other contains four electrons. Therefore here one expects the appearance of an additional electrostatic repulsion, whose energy may contribute significantly to the energy of the $^3\Sigma \rightarrow {}^1\Delta$ excitation, which is 23 kcal mole^{-1}.[17]

The addition of electrons to the oxygen molecule leads to the population of antibonding orbitals, which entails a decrease of the O–O bond order. The observed changes in bond length and vibrational frequency confirm the existence of this tendency (Table 1).

Table 1. Characteristics of the O–O bond strengths.

Species	Calc. bond order	Bond length, Å	Stretching vibration frequency, cm^{-1}	References
O_2	2	1.21	1555	18,19
O_2^-	1.5	1.28 (KO_2)	1089	20,21
O_2^{2-}	1	1.49 (BaO_2)	880 (H_2O_2)	20,19

According to the results of *ab initio* MO SCF calculations, the $2\sigma_g$, $2\sigma_u^*$, and $3\sigma_g$ orbitals in different dioxygen species are mixed[22]. The directional character of hybrid orbitals in space is known[23] to be more marked compared with that of non-hybrid orbitals, which ensures a higher degree of overlapping on formation of σ bonds, in particular when the orbitals of both interacting species are hybridised. Furthermore, hybridisation leads to a decrease of the repulsion of the lone electron pairs. Therefore the ethylene-like reactive forms $O_2(^1\Delta)$, O_2^-, and O_2^{2-} with sp^2 hybridisation of the orbitals can play a definite role in complex formation.

III. THE NATURE OF ACTIVATING BINDING

The principle of the conservation of spin can impose limitations on the nature of the elementary processes in chemical reactions[8]. By virtue of spin conservation the interaction of the oxygen molecule in the triplet state with a molecule in the singlet state cannot lead to the formation of molecules in singlet states only. From this it follows that oxygen in the ground state is not a heterolytic (two- or four-electron) oxidant and reacts preferentially as a homolytic (one-electron) oxidant.

The main types of homolytic oxidation reactions occurring with conservation of spin are as follows:

(a) reaction with a molecule:

$$\overset{\uparrow\downarrow}{R}H + \overset{\uparrow\uparrow}{O_2} = \overset{\uparrow}{R} + \overset{\uparrow\downarrow\uparrow}{HO_2} \quad ;$$

(b) reaction with a radical

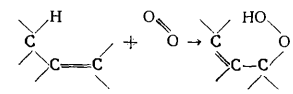
$$\overset{\downarrow}{R} + \overset{\uparrow\uparrow}{O_2} = \overset{\downarrow\uparrow\uparrow}{RO_2} \quad .$$

As a result of a termolecular homolytic reaction in which the oxygen molecule abstracts one hydrogen atom from each of two substrate molecules, the spin is also conserved[24,25]:

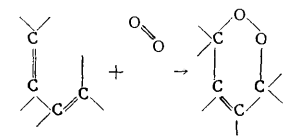
$$\overset{\uparrow\downarrow}{R}H + \overset{\uparrow\uparrow}{O_2} + \overset{\uparrow\downarrow}{R}H = \overset{\uparrow}{R} + \overset{\downarrow\uparrow\downarrow\uparrow}{HOOH} + \overset{\uparrow}{R} \quad .$$

The above homolytic reactions are difficult because they all occur with participation of free radicals, whose equilibrium concentration is as a rule very low under normal conditions.

In order to achieve the reaction without the involvement of free radicals, it is necessary to excite the oxygen molecule to the singlet state, for which, from the standpoint of spin conservation, it can react as a two-electron non-homolytic oxidant:



or



The formation of complexes by the oxygen molecule with transition metal compounds leads to a change in its spin state and in the nature of its reactivity. The activating effect of transition metal complexes is associated with the presence of closely spaced *d* levels of the metal ions, which are responsible for the ready formation of activated forms of different multiplicity.

When the oxygen molecule reacts with a doublet centre, a radical complex, capable of vigorous interaction not only with radicals but also with singlet molecules, can be formed:

$$\overset{\downarrow}{M} + \overset{\uparrow\uparrow}{O_2} = \overset{\downarrow}{M} \cdot \overset{\uparrow\uparrow}{O_2} \quad .$$

The interaction with a triplet centre can lead to the formation of a complex of singlet oxygen. It is assumed that a complex of triplet oxygen is formed in the first stage of the process. As a result of the change in molecular symmetry on complex formation, the energy degeneracy of the π_d^* orbitals is lifted, which facilitates the transition of the molecule to the singlet state:

$$\overset{\downarrow\downarrow}{M} + \overset{\uparrow\uparrow}{O_2} = \overset{\downarrow\downarrow}{M} \cdot \overset{\uparrow\uparrow}{O_2} = \overset{\downarrow\uparrow}{M} \cdot \overset{\downarrow\uparrow}{O_2} \quad .$$

The role of the triplet states of transition metal complexes in such processes is indicated by studies on the sensitised photoexcitation by molecular oxygen[26].

Coordination interaction alters the electronic structure of the molecule owing to the change in the population and disposition of its orbitals. The transition metal can withdraw electron density from certain bonding orbitals and shift it to certain antibonding orbitals, which is analogous to the electronic excitation of the free molecule. In terms of interatomic distances and valence angles, the coordinated molecule can resemble various activated forms of the free molecule[27]. A characteristic feature of this type of excitation is that it occurs solely due to the

coordination interaction with the metal atom without the external supply of energy. The heats of such complex formation processes are as a rule low, but the processes lead to considerable chemical changes in the coordinated ligand.

It is believed that the most significant factor in the activating complex formation between transition metal compounds and the oxygen molecule is its interaction with the metal atom, since in this case the specific role of the latter, associated with the presence of *d* valence states of different symmetry and spatial orientation, has the greatest effect. However, the nature of the ligand environment, whose influence extends via the metal atom to the coordinated molecule, is very important. Nor can one rule out the possibility of the activation of the oxygen molecule by its outer-sphere coordination[28].

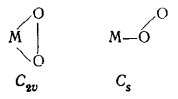
Evidently, apart from the electronic factor, the geometrical factor has an effect in the interaction between the dioxygen molecule and the activator, because definite steric hindrance to the binding of the oxygen molecule can probably lead to a definite strain in the bonds of the molecule and hence to a definite type of reactivity[29].

IV. THE STRUCTURE OF DIOXYGEN COMPLEXES

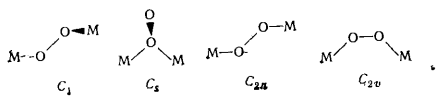
In the reaction with transition metal complexes the oxygen molecule behaves mainly as an electron acceptor, as shown by the results of studies using different methods (X-ray photoelectron spectroscopic[30,31], thermodynamic[32], and electrochemical[33]). The electron-donating capacity of the metal (the energy of the occupied *d* orbitals) can play a significant role in the binding of oxygen. Complexes with oxygen are usually formed by compounds of transition metals in the lowest oxidation state, which exhibit a sufficient electron-donating capacity to ensure charge transfer but not high enough to cause the dissociation of the O–O bond.

The nature of the binding of oxygen in the complex and the reactivity of the coordinated molecule are usually considered on the basis of the geometry of the oxygen adduct, since evidently the latter determines the state of oxygen in the complex and hence possibly also the type of reactivity of the bound oxygen.

Mononuclear complexes with different symmetries of the metal–dioxygen fragment—the closed (C_{2v}) and open (C_s) types—are known:



Furthermore, there are dinuclear complexes which can be regarded as structural derivatives of mononuclear complexes of the open type:



In mononuclear complexes of the open type and in the corresponding dinuclear derivatives the MOO valence angles are close to 120°, i.e. these configurations are apparently based on the state of the oxygen atom with sp^2-hybridised orbitals.

No dioxygen complexes known to have a linear configuration of the metal–dioxygen fragment have yet been obtained; this distinguishes them from the complexes of molecular nitrogen in which linear coordination is most typical. Probably in this case the different populations of the antibonding orbitals and hence the different molecular symmetries have an effect. In the nitrogen molecule there are two vacant π orbitals, which accept two pairs of *d* electrons from the metal and this favours the formation of a linear structure[34]. In the oxygen molecule there can be only one vacant π orbital (in the $^1\Delta$ state) which can accept only one pair of *d* electrons and this rules out a linear coordination in this case.

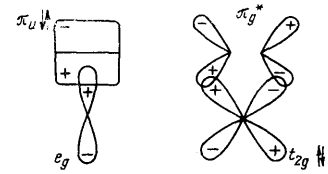


Figure 2. Griffith's model of a π-complex.

The formation of a dioxygen complex of the closed type may resemble the binding in olefin complexes[35], as pointed out by Griffith[36]. It is suggested that a σ bond is formed via an occupied π-bonding molecular orbital of oxygen and a vacant *d* orbital of the metal. Furthermore, there is a possibility of forming a π bond from the lone pair of *d* electrons of the metal atom and an antibonding orbital of the oxygen molecule (Fig. 2). Thus the energy splitting of the degenerate oxygen π^* orbitals in the ligand field of the complex is postulated.

Presumably when the degree of charge transfer from the metal to oxygen is fairly pronounced, the structure of the complex is best described by the model of a doubly coordinated σ complex, which may be important in the determination of the reaction mechanisms. The structural characteristics of a number of mononuclear complexes are presented in Table 2.

Table 2. Structural data for dioxygen complexes of the closed type (diamagnetic).

Compound	M–O bond length, Å	O–O bond length, Å	Type of addition	References
$[Co(Ph_2PCH{=}CHPPh_2)_2 \cdot O_2]BF_4 \cdot 2C_6H_6$	1.871; 1.902	1.420	irrev.	37
$[Rh(Ph_2PCH_2CH_2PPh_2)_2 \cdot O_2]PF_6$	2.026	1.418	rev.	38
$[Ir(Ph_2PCH_2CH_2PPh_2)_2 \cdot O_2]PF_6$	1.961; 1.990	1.625	irrev.	38
$Ir(PPh_3)_2Cl(CO)O_2$	2.04; 2.09	1.30	rev.	39
$Ir(PPh_3)_2Br(CO)O_2$	—	1.36	rev.	37
$Ir(PPh_3)_2I(CO)O_2$	2.035; 2.082	1.509	irrev.	40
$Ir(PPh_2Et)_2Cl(CO)O_2$	2.036; 2.084	1.461	rev.	41
$Pt(PPh_3)_2O_2 \cdot 1.5C_6H_6$	2.01	1.45	irrev.	42
$Pt(PPh_3)_2 \cdot O_2 \cdot 2CHCl_3$	2.006	1.505	irrev.	43

The influence of the metal can be estimated from experimental data for the structures of the cationic complexes of cobalt, rhodium, and iridium with bis(diphenylphosphinoethane) and bis(diphenylphosphinoethylene) ligands. The iridium atom is capable of forming a

stronger M–O bond than the rhodium atom and also of loosening the O–O bond (Table 2). This is attributed to the fact that the π-donor metal orbitals in the iridium complex must lie above those in the rhodium complex[38-44]. Neglecting the effect of the change of ligand, we may note that the observed sequence of changes in the $M-O_2$ bond lengths is consistent with the sequence of changes in the kinetic and activation parameters of the binding of oxygen by the bis(diphenylphosphinoethylene) complexes[44]. The difference between the energies of the *d* orbitals of the corresponding metal complexes probably plays a role here. The specificity of the bis(diphenylphosphinoethylene) ligand may be reflected in this series by the absence of a correlation between the M–O bond lengths on the one hand and the O–O bond lengths on the other.

It is noteworthy that the O–O bond length is very sensitive to changes in the ligand environment of the metal. As the auxiliary ligands become less electronegative (Cl > Br > I; PPh_3 > PPh_2Et), the O–O distance increases. A correlation is also observed between the O–O bond length and the degree of reversibility of the binding of oxygen. This can be explained by the fact that, with increase of the energy of *d* orbitals, the effect of the donation of π electrons to the antibonding molecular orbital is enhanced.

The O–O stretching vibration frequency in the spectra of complexes of the given type is greatly reduced compared with that for the free molecule, to a value of the order of 800–900 cm^{-1}.[45,46] The M–O stretching vibration frequency is in the range 450–600 cm^{-1}. A satisfactory correlation between these frequencies and the changes in the structural parameters of the compounds has not so far been obtained.

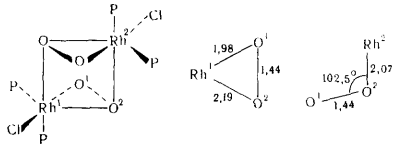


Figure 3. The structure of $[Rh(Ph_3P)_2ClO_2]_2$ (the bond lengths are given in Å).

The dinuclear diamagnetic complex $[Rh(PPh_3)_2ClO_2]_2$, in which two oxygen molecules are combined reversibly[47], is unusual (Fig. 3). Its unusual feature is that each oxygen molecule, which behaves as a bridging ligand, forms a coordinate bond of the closed type with one metal atom, behaving as an equatorial ligand, while the coordinate bond formed with the other metal atom is of the open type and oxygen behaves as an axial ligand. Each coordinated oxygen molecule forms two σ bonds: one via the occupied π_u orbital of oxygen and the vacant equatorial dsp^3 orbital of one metal atom and the other via the occupied nonbonding hybrid orbital of oxygen (*p* orbital with some *s* character) and the vacant axial dsp^3 orbital of the other metal atom. Furthermore, many-centre π bonding is postulated. This complex can be regarded as an intermediate structural type in relation to complexes of the open and closed types.

It is interesting that the coordinated oxygen molecule acquires the ability to form hydrogen bonds[43]. In the complex $Pt(PPh_3)_2O_2.2CHCl_3$ the hydrogen atoms of the solvate molecules are in the same plane as the Pt and O atoms, so that the PtOH angle is 180° and the O–H distance is 2.04 Å (Fig. 4). Compared with the benzene solvate, which shows no signs of the formation of hydrogen bonds, the O–O bond length is appreciably increased, while the M–O bond hardly changes (Table 2). It is so far not clear how the bond with the solvent species is formed: as a result of the excitation of the oxygen molecule or as a result of the excess negative charge on oxygen. The location of the hydrogen atoms in the same plane as the metal–dioxygen fragment suggests that the oxygen orbitals which form the $Pt-O_2$ bond are involved in hydrogen bonding, but the slight change in the Pt–O bond is not entirely consistent with this hypothesis.

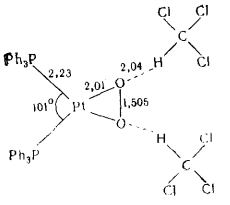


Figure 4. The formation of a hydrogen bond (the bond lengths are given in Å).

The complex $IrCl(PPh_3)_2(C_2H_4)O_2$, in which the simultaneous coordination of oxygen and ethylene has been demonstrated by infrared spectroscopy and NMR[48] (Fig. 5), can serve as a model of homogeneous catalytic oxidation.

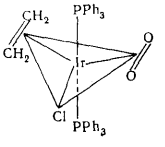
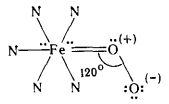


Figure 5. The proposed structure for $IrCl(PPh_3)_2(C_2H_4)O_2$.

The paramagnetic complex $Ru(AsPh_3)_2Cl_2O_2$ should probably be assigned to the same structural type in view of the appearance of the 880 cm^{-1} band in the infrared spectrum[49]. Another paramagnetic complex, $Cr[N(i\text{-}Pr)_2.]_3O_2$, has an effective magnetic moment of 2.03 Bohr magnetons (B.M.) and a vibrational frequency of 980 cm^{-1},[50] which indicates the possible characteristics of its structure.

Aleksandrov et al. recently demonstrated the possibility of the formation of oxygen complexes with organic derivatives of post-transition metals[51]: the "reversible" adduct $Et_2Cd.2O_2$, with an intense 790 cm^{-1} band in its infrared spectrum, was obtained. The transfer of the π_g electron pair of oxygen to the vacant 5*s* or 5*p* orbital of the metal and also the interaction via the occupied 4*d* orbitals of the metal and the vacant π_g orbital of oxygen can make a definite contribution to bond formation on complex formation.

The iron complex with porphyrin and histidine, having the configuration of a tetragonal pyramid, is the active centre for the binding of oxygen in haemoglobin and myoglobin[52]. The planar porphyrin ligand is located at the base of the pyramid, the bivalent iron ion coordinated to four nitrogen atoms being in the centre. The apex of the pyramid is occupied by the tertiary nitrogen atom of histidine and the oxygen molecule adds to the base of the pyramid. The orientation of the dioxygen group relative to the iron atom has not so far been determined experimentally. According to Pauling[53], the structure of the coordination centre of oxyhaemoglobin can be represented as follows:



It is believed that the tervalent oxonium ion with sp^2-hybridised orbital is involved in the formation of a bond. From the standpoint of the molecular orbital method, this structure can be regarded as a π-bonded complex of the open type.

According to Griffith, the oxygen in oxyhaemoglobin is coordinated as in a complex of the open type[36]. Since in this case the iron ion must have a coordination number of seven, one may expect the occurrence of steric hindrance[54]. So far no model compound with a similar configuration has been obtained.

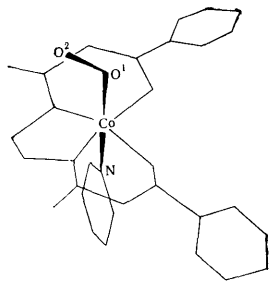


Figure 6. The structure of Co(bzacen)(pyridine)O_2.

The orientation of the coordinated molecule relative to the metal atom proposed by Pauling has been demonstrated for the tetraphenylporphyrin complex of cobalt with NO,[55] which is isoelectronic with the porphyrin complex of iron with oxygen. A similar orientation of the dioxygen group was established for Co(bzacen)(pyridine)O_2,[56] where bzacen is *NN'*-ethylenebis(benzoylacetoniminide) (Fig. 6). One should note that in these molecular structures the projection of the coordinated molecule onto the plane of the equatorial ligand lies between the adjacent bonds of the metal in the equatorial plane. The staggered conformation probably corresponds to minimum repulsion of the non-bonded atoms. However, this disposition of the dioxygen group should decrease the effectiveness of π-bonding since the maximum overlap of the oxygen p orbital with one of the metal t_{2g} orbitals may be expected for the eclipsed conformation[12,57]. The unusual conformation of oxygen can be one of the factors determining the possibility of the reversible binding of oxygen to haemoglobin.

Three types of dioxygen compounds of cobalt, in which the coordinated oxygen molecule forms an obtuse CoOO angle, are distinguished: mononuclear paramagnetic, dinuclear diamagnetic, and dinuclear paramagnetic (Table 3).

Mononuclear complexes are formed on direct interaction between certain bivalent cobalt compounds and oxygen. Their magnetic moments are 1.85 ± 0.35 B.M., which is evidence for the presence of one unpaired electron in the complex[65,66]. According to ESR studies[67-71], the unpaired electron is located in an orbital having 10–20% of metallic character, i.e. is localised preferentially at the dioxygen group. X-Ray photoelectron spectroscopic[31] and thermodynamic studies[32] suggest that the charge state of the metal corresponds more closely to cobalt(III) than to cobalt(II). The bond with the oxygen molecule can arise as a result of spin pairing and electron transfer from the metal atom to oxygen. The coordinated molecule has the character of the molecular ion O_2^-, forming a donor–acceptor bond with the tervalent cobalt atom via the sp^2-hybridised lone electron pair with some delocalisation of the unpaired electron over the metal[65,66,72]. In mononuclear complexes of this type the O–O interatomic distance (1.26 Å)[56] and the O–O stretching vibration frequency (1120–1140 cm^{-1})[66] correspond to the structural parameters of the O_2^- ion (Table 1).

The presence of an additional electron in the mononuclear cobalt analogues of oxyhaemoglobin can be responsible for some of its structural characteristics. Since the iron atom in oxyhaemoglobin has a stable 18-electron inert gas shell, the additional electron must be located in an oxygen orbital. Owing to the high energy of the vacant $3\sigma_g$ orbital, the electron interacts with the π_g orbital, displacing the electron pair involved in the dative π interaction on the metal side. Thus a considerable weakening of the π-bonding component may be expected in cobalt analogues of oxyhaemoglobin as compared with oxyhaemoglobin itself.

Apart from the mononuclear complexes, fairly numerous dinuclear oxygen complexes of cobalt are known. Assuming the formation of covalent bonds between cobalt ions and the oxygen molecule, it is believed that the latter undergoes a two-electron reduction[13]. The resulting dinuclear complex can be regarded as a coordination compound of the peroxide type: $Co^{III} \leftarrow O_2^{2-} \rightarrow Co^{III}$.

The dinuclear coordination of the peroxide anion can be achieved in two ways: by the addition to each oxygen atom of one metal atom (C_1) or by the addition of both metal atoms to one oxygen atom (C_S).

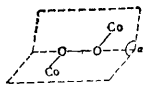
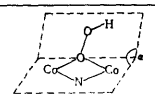
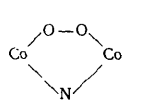
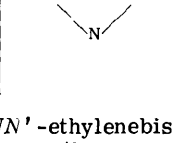
The one-electron oxidation of the diamagnetic complexes leads to the corresponding paramagnetic compounds. As for the mononuclear complexes, there is a tendency towards the retention by the metal of the stable 18-electron shell, i.e. an electron must be removed from the dioxygen group:

$$Co^{II} \leftarrow O_2^{2-} \rightarrow Co^{III}—\bar{e}=Co^{III} \leftarrow \dot{O}_2^- \rightarrow Co^{III} \quad .$$

ESR spectra confirm the preferential location of the unpaired electron in the dioxygen group[73]. In contrast to the diamagnetic complexes, the metal–dioxygen fragment in the dinuclear paramagnetic complexes has a planar structure (C_{2h}), in accordance with its superoxide character.

The data presented in Table 3 show that, as the π-bonding electron pair is transferred towards the dioxygen group, the strength of the M–O bond increases and that of the O–O bond falls. The changes in the valence angles

Table 3. Structural data for dioxygen complexes of cobalt.

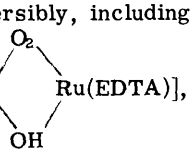
Structural type	Configuration of the metal-dioxygen group	Compound	Co-O bond length, Å	O-O bond length, Å	Angles: CoOO	Angles: others	Type of addition	References
$Co^{III} \leftarrow \dot{O}_2^-$ (paramagnetic)		Co(bzacen)(pyridine)O_2*	1.88	1.26	126	—	rev.	56
$Co^{III} \leftarrow O_2^{2-} \rightarrow Co^{III}$ (diamagnetic)		(H_2O) (3F— Salen) CoO_2Co(3F—Salen)** $+ 2CHCl_3 + C_6H_{11}$	2.000 1.931	1.308	119 117	$\alpha = 122$	rev.	58
		(DMF)(Salen)CoO_2Co(Salen)(DMF)***	1.910	1.338	120	$\alpha = 110$	rev.	59
		$[(NH_3)_5CoO_2Co(NH_3)_5](SO_4)_2$	1.882	1.47	112	$\alpha = 146$	irrev.	60
		$(NO_3)_4 \cdot 2H_2O$	1.92	1.42	<129	CoOCo= =102 $\alpha < 180$	irrev.	61
$Co^{III} \leftarrow \dot{O}_2^- \rightarrow Co^{III}$ (paramagnetic)		$[(NH_3)_5CoO_2Co(NH_3)_5] \cdot SO_4(HSO_4)_3$	1.894	1.312	117	—	irrev.	62
		$[(NH_3)_5CoO_2Co(NH_3)_5] \cdot (NO_3)_5$	1.895	1.317	117	—	irrev.	63
		$\cdot (NO_3)_4$	1.867	1.320	121	—	irrev.	64
		 $(NO_3)_4 \cdot H_2O$	1.88	1.36	119	—	irrev.	61

* bzacen = *NN'*-ethylenebis(benzoylacetoniminide) (Ed. of Translation).
** 3F-Salen = bis-(3-fluorosalicylidene)ethylenediamine (Ed. of Translation).
*** Salen = bis-salicylidene-ethylenediamine (Ed. of Translation).

of the $Co-O_2-Co$ groups can be accounted for by a change in the character of the orbitals involved in the binding of the oxygen molecule.

X-Ray diffraction studies have established that the orientation of the dioxygen group relative to the equatorial ligand is the same as for the mononuclear complexes.

Dinuclear compounds of other transition metals are known, in which the oxygen is bound reversibly, including



the diamagnetic complex $K_2Na[(EDTA)Ru(O_2)Ru(EDTA)(OH)]$, obtained by Ezerskaya and Solovykh[74,75], where EDTA is the tetrabasic residue of ethylenediaminetetra-acetic acid, and the paramagnetic complex $[Mn(Salen\dagger)]_2O_2$, whose effective magnetic moment is 2.79 B.M.[76]

The role of the specific ligand environment of the metal in biological oxygen carriers is manifested by a change in the thermodynamic parameters of the oxygenation process[77-85].

The differences between the stabilities of the oxygen complexes of cobalt with different equatorial ligands (for example TMPP and Salen, Table 4) are probably due to the differences between the π-acceptor capacities of these equatorial ligands. π-Conjugated macrocyclic systems do not as a rule promote strong binding of oxygen. For certain complexes with the same type of ligand environment, ΔG° may be correlated with pK_a for the axial ligand. A decrease in the stability of the mononuclear oxygen complex with sterically hindered axial ligands (2,6-lutidine, 2,4,6-collidine, and quinoline) has been noted. The sterically hindered groups in the ligand prevent its effective approach to the metal, weakening the stabilising *trans*-influence on the metal–oxygen bond. As a result of the distortion of the configuration, the stability of the dinuclear compound may be reduced[84]. For a rigidly bound equatorial ligand of the type of porphyrin, the importance of steric hindrance of the coordination of the axial ligand increases[81].

† See Table 4 (Ed. of Translation).

Table 4. Thermodynamic characteristics of the reversible binding of oxygen in solution by cobalt complexes ($CoII + O_2 = CoO_2$).[82,83]

Ligand: equatorial	Ligand: axial	Standard state	ΔG°, kcal mole^{-1}	ΔH°, kcal mole^{-1}	ΔS°, e.u.
Dibasic residue of tetra-4-methoxyphenylporphyrin (TMPP)	Pyridine	$P_{O_2} = 1$ atm, $T = 208°$	−0.50	−9.3	−42
	4-Picoline		−0.75	−8.8	−39
	2,4,6-Collidine		−0.09	−8.5	−45
Dibasic residue of bis-salicylidene-ethylenediamine (Salen)	Pyridine	$P_{O_2} = 1$ atm, $T = 298°$	−0.80	−16.7	−54
	4-Picoline		−0.87	−17.0	−54
	2,6-Lutidine		−0.67	−18.3	−59
	Quinoline		+0.03	−15.2	−51

V. MATRIX FIXATION OF OXYGEN

The stabilisation of the oxygen-fixing centre of haemoglobin is probably promoted by the matrix effect. The basic unit of haemoglobin is the planar tetracoordinate complex of iron(II) and protoporphin. The haemoglobin

molecule contains four haem groups, which are linked by peptide chains via histidine to the protein moiety. Each of the four protein chains forms a fairly complex three-dimensional structure around the haem in such a way that the latter is located in a fold of the protein chain (matrix) within which oxygen may be bound.

In accordance with Pauling's hypothesis[53], it is believed that the terminal atom of the coordinated oxygen molecule, which carried an excess negative charge, is oriented towards the NH group of distal histidine, forming a hydrogen bond. Thus a two-point fixation of the molecule is achieved by a cooperative interaction with the metal complex and with the histidine group of the protein (Fig. 7).

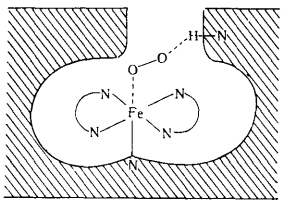


Figure 7. A model of the matrix fixation of oxygen by haemoglobin.

Presumably the matrix effect plays a dual role: firstly it prevents the irreversible interaction of molecular oxygen with the active component of haemoglobin and secondly it rules out the possible oxidation of labile substrates.

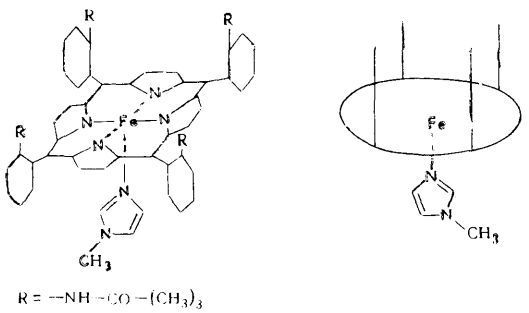


Figure 8. The unit of a matrix with artificial steric hindrance and a schematic representation of the element.

Definite information about the occurrence of the matrix principle in the fixation of molecular oxygen can be provided by a study of the binding of oxygen in synthetic models. A number of approaches to the creation of models based on the matrix principle may be noted. In the first case the model is formed by the incorporation of an analogue of the active centre in the polymer being formed. A cavity should be created over the active centre. The cavity is usually produced by incorporating in the polymer a model compound in which a small molecule, particularly CO, is reversibly combined. After the formation of the polymer, the small molecule is removed (by flushing with an inert gas).[29,86]

The second approach involves the creation of artificial steric hindrance around the active centre[87] (Fig. 8).

Apart from the creation of artificial steric hindrance, the elements of matrix systems can be formed by employing the conformations of the ligand environment[88] (Fig. 9). According to certain observations[88], the steric hindrance influences the stability of the adduct of molecular oxygen with the metal complex.

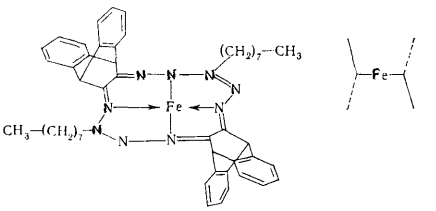


Figure 9. A model of the matrix formed as a result of the conformation of the ligand environment and a schematic representation of the model.

However, the matrix effect can be shown under certain conditions even in the absence of steric hindrance, when one employs a model in which there is an appreciable cooperative interaction with the ligand environment[89,90] (Fig. 10). The cooperative interaction in matrix systems has a definite advantage over simple complexes which are haemoglobin analogues. According to the results of Cheng and Traylor[86], there is a very significant difference between the degrees of binding of molecular oxygen to the iron(II) complex in which the *trans*-ligand (pyridine) is coordinated to the iron ion only and the analogous complex in which pyridine is additionally linked to the equatorial ligand (Fig. 10).

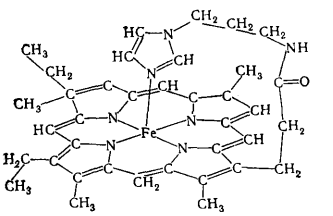


Figure 10. A model of the matrix with an independent linkage between the axial and equatorial ligands.

Together with a change in reactivity, one can also expect a change in selectivity when the *trans*-ligand is replaced; this has been confirmed by studies on the binding of carbon monoxide and molecular oxygen. In particular, these results show that, when imidazole in the *trans*-position is replaced by pyridine, the system loses its ability to bind oxygen[86].

Furthermore, the results of studies involving similar systems lead to the conclusion that the coordinated oxygen molecule is additionally stabilised when there is a possibility of the formation of a hydrogen bond with fragments of the system (two-point fixation)[86].

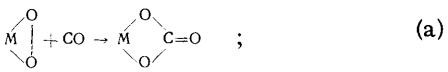
Coboglobins apparently occupy a special place among matrix systems[91,92], since the protein moiety is fully retained in their structure. Consequently the study of the binding of oxygen by coboglobins can elucidate the role of the protein moiety in this process.

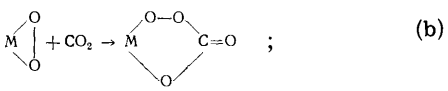
Furthermore, the employment of such systems as haemoglobin analogues makes it possible to elucidate certain characteristics of the influence of the metal on the effects accompanying the addition of the oxygen molecule (the phosphate effect, the Bohr effect, and *gem–gem* interaction). In particular, a definite difference has been observed[92] between the *gem–gem* interactions in coboglobin and haemoglobin during the binding of oxygen.

VI. REACTIVITY OF THE COORDINATED MOLECULE

Two main types of reactions of the complexes are distinguished: the inner-sphere interactions with preliminary coordination of the substrate in the inner sphere and the outer-sphere interactions where there is no inner-sphere coordination of the substrate. Evidently in the first case both oxygen and the substrate are activated, while in the second case only oxygen is activated.

The reactions can be stoichiometric or catalytic. The addition of small molecules to the dioxygen complexes of Group VIII metals must be classified as stoichiometric oxidation reactions[93–99]:


(a)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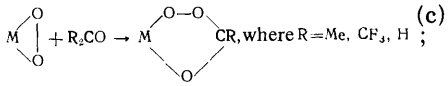
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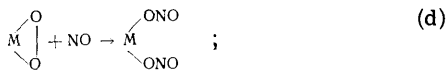
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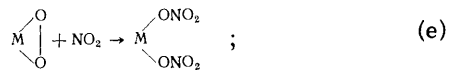
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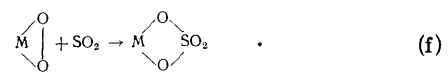
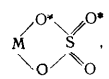
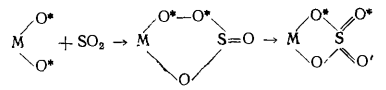

(f)

All the reactions with coordination-unsaturated platinum complexes take place readily and probably involve an inner-sphere mechanism[100]. The coordination-saturated rhodium and iridium compounds react only with NO_2 and SO_2, i.e. molecules in which the aprotic acid properties are most pronounced. In these cases one might postulate a mechanism involving a simple outer-sphere addition. However, studies with isotopically labelled oxygen in the complex have shown that the label is distributed in the product in the following manner:



i.e. the dissociation of the O–O bond is accompanied by the dissociation of the M–O bond[101]. The electrophilic attack by SO_2 is probably directed to the negatively charged oxygen atom, facilitating the heterolytic dissociation of the M–O bond with subsequent insertion of the SO_2 molecule in this bond and a further rearrangement of the resulting peroxide complex:

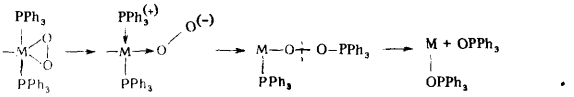


Oxygen π complexes of the closed type catalyse the oxidation of tertiary phosphines to the corresponding oxides[91,102–104] and also of isocyanides to isocyanates[45]. Since the substrates undergoing oxidation can function as specific π-acceptor ligands, presumably the reactions have an inner-sphere mechanism. According to the results of kinetic studies, all the intermediate complexes contain substrate molecules and have an 18-electron coordination sphere (Table 5), which is specific to inner-sphere catalysis according to Halpern's hypothesis[105].

Table 5. Characteristics of the intermediate complexes.

Composition	No. of coordinated ligands	No. of electrons in valence shell of metal	References
$Ru(O_2)(SCN)(NO)(PPh_3)_3$	6	18	104
$Ir(O_2)(I)(CO)(PPh_3)_2$	5	18	38
$Pt(O_2)(PPh_3)_3$	4	18	95

A remarkable reaction is catalysed by a ruthenium complex. According to infrared spectroscopic data[104], the coordination of the oxygen molecule in the initial 16-electron compound $Ru(O_2)(SCN)(NO)(PPh_3)_3$ is of the closed π-complex type, i.e. the coordination number is probably six. The addition of the PPh_3 molecule leads to the formation of a sterically strained configuration with a coordination number of seven, which can promote the inner-sphere *cis*-migration of the ligand with a change in the orientation of the dioxygen group relative to the metal atom:



In the general case there is also a possibility of an inner-sphere mechanism with a simultaneous transfer of two ligands.

The electronic factor can determine the possibility of the inner-sphere oxidation reaction for a specific geometry of the complex. The latter should probably also ensure both definite relative positions of the oxygen and reacting ligand molecules and a definite stoichiometry (in particular for concerted reactions).

The lack of data precludes an adequately detailed discussion of the interesting reaction involving the catalytic hydrogenolysis of molecular oxygen in the presence of a number of complexes[106]. However, it is known that oxygen-fixing complexes can accelerate the autoxidation of

hydrocarbons[107-111]. Reactions of this type can proceed via an outer-sphere mechanism, since they have certain features of radical-chain processes, in particular they are retarded in the presence of specific inhibitors. It is also possible that in some cases the initiating effect of the metal complexes is not associated with the activation of molecular oxygen but with the acceleration of the decomposition of the hydroperoxides arising in the oxidation of the substrate[71-111]. However, the sensitisation of molecular oxygen by the complex appears to be more probable in many cases[109]. It has been noted[110] that complexes in which oxygen is least strongly bound exhibit the highest activity in the autoxidation of styrene. It is suggested that the sensitising species in such reactions may be a mononuclear complex of the superoxide type[11]:

$$M^{n+} + O_2 \rightarrow M^{(n+1)} + \dot{O}_2^- \xrightarrow{RH} M^{(n+1)} + OOH^- + R\cdot \ ;$$

$$M^{(n+1)} + OOH^- \rightarrow M^{n+} + HOO.$$

Mononuclear cobalt complexes of the superoxide type have been used as model compounds for the investigation of the mechanism of outer-sphere oxidation reactions. The ESR signal of the oxygen complex of corrinoid [Co^{II}(vitamin B_{12})] in the presence of small amounts of one-electron reducing agents (hydroquinone, *p*-phenylenediamine, ascorbic acid, and thiols) is replaced by the signal of the radical of the oxidised substrate, i.e. a one-electron oxidation–reduction reaction takes place between the oxygen complex and the substrate[71]. In the presence of excess reducing agent cobalt(II) is regenerated and the corresponding catalytic reaction occurs.

Table 6. Polarographic reduction of oxygen complexes[33].

Compound	Half-wave potential, V	Medium, reference electrode
(DMF) (*o*-Phenylenesalen)Co(O_2)	-0.300	DMF, Ag|AgCl, KCl
(DMF) (3-CH_3O-Salen)Co(O_2)	-0.324	Ditto
(DMF) (Salen)Co(O_2)	-0.420	"
(DMF) (acacen)Co(O_2)	-0.520	"
(Pyridine) (*o*-Phenylenesalen)Co(O_2)	-0.656	Pyridine, sat. cal.e-de
(Pyridine) (3-CH_3O-Salen)Co(O_2)	-0.660	Ditto
(Pyridine) (Salen)Co(O_2)	-0.660	"
O_2	-0.810	DMF, Ag|AgCl, KCl
O_2	-0.836	Pyridine, sat. cal.e-de

* *o*-Phenylenesalen = *o*-phenylenebis-salicylidene-ethylenediamine (Ed. of Translation).
** Salen = bis-salicylidene-ethylenediamine (Ed. of Translation).
*** acacen = *NN'*-ethylenebis(acetylacetoniminide) (Ed. of Translation).

It follows from the results of polarographic studies[33] that paramagnetic cobalt complexes of oxygen are more powerful one-electron oxidants than free oxygen or the initial non-oxygenated cobalt(II) species. The half-wave potential corresponding to the reversible one-electron reduction of the oxygen complex decreases as the electron-donating effect of the ligand environment of this metal becomes enhanced. Both the equatorial and the axial ligand then have an effect. For a more basic *trans*-ligand (pyridine), the electron-donating effect of the equatorial ligand is not differentiated (Table 6).

It follows from the data in Table 6 that the transfer of the negative charge from the metal atom to oxygen decreases the oxidising capacity of the oxygen complex, which can be readily understood within the framework of a simplified model postulating the location of the unpaired electron at the dioxygen group. Since the metal atom has a filled 18-electron shell and the oxygen has an accessible half-filled orbital, the reducing electron must occupy the latter. Evidently the energy of this orbital depends on the effective charge of the dioxygen group. Therefore the addition of the electron will be hindered by energy factors when the dioxygen group has an excess negative charge. In this case the most labile oxygen complexes, in which the M–O_2 bond is largely covalent, should exhibit the greatest oxidising capacity.

The results show that the labile mononuclear complex (PPh_3)(Salen)Co(O_2) can give rise to non-chain catalytic oxidation of aliphatic alcohols under mild conditions[112].

Thus two extreme types of active structures are characteristic of mononuclear oxygen complexes. They differ in the nature of the relative orientation of the oxygen molecule and the metal atom, in the degree of π-bonding, and in the spin state: they are diamagnetic π-complexes of the closed type and paramagnetic σ-complexes of the open type. The coordinated oxygen molecule in the diamagnetic complex bears some similarity to the oxygen molecule in the singlet state, which can account for its involvement in inner-sphere reactions of the non-radical type. In the paramagnetic complex the coordinated molecule resembles the active superoxide radical, and this is the reason for the occurrence of outer-sphere reactions of the radical type. Apart from these extreme structures, definite information about the nature of the activation of the molecule can be provided by structures of intermediate type.

It has been shown[49] that the high-spin complex $Ru(AsPh_3)_2Cl_2O_2$ readily combines with an SO_2 molecule, forming the corresponding sulphate, like a low-spin π-complex. The unpaired electrons are in this case probably located at the metal and the coordinated dioxygen group is spin-paired, i.e. the reactivity of the complex is determined by the state of the coordinated molecule and not of the metal atom.

There is so far no information about the nature of the reactivity of diamagnetic complexes of the open type. Presumably the coordinated oxygen molecule can exhibit a hydride acceptor activity.

It is known that dinuclear cobalt complexes are capable of oxidative combination with SO_2 and NO_2 molecules[113,114], but the mechanisms of these interesting reactions have not been elucidated.

The problem of creating an artificial matrix catalyst, an analogue of an oxidase-type enzyme, is extremely urgent. It was established recently[115] that the polymeric ligand poly-4-vinylpyridine causes a sharp increase of the catalytic activity of copper ions in the autoxidation of ascorbic acid. Although the interpretation of this effect is at present difficult, studies of this kind appear promising. The problem of the synthesis of the catalytic matrix can be solved on the basis of the specific sorption effect by obtaining "imprints" of the surface of the solid with the given orientation of the substrate molecule relative to the active centre[116].

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Studies on the activation of molecular oxygen have been recently carried out mainly using biological models for the fixation of molecular oxygen. They have yielded many

new data. Calculation by the Hückel molecular orbital method[117] on the fragment M–O_2–M, where M is an element of the first transition series ranging from titanium to nickel (there is an analogy with dinuclear dioxygen complexes), yielded some information about the specific role of the metal and also about the nature of the binding of the dioxygen group. The calculation demonstrated that the population of the M–O_2 bond is a maximum in the middle of the series of 3*d* complexes. This variation is determined by the fact that the overlap integrals of the d_{yz} and p_y orbitals decrease on passing from titanium to nickel and the coefficient defining the contribution of the d_{yz} orbital to the bonding molecular orbital increases in the same direction.

It has been suggested on the basis of calculations that σ-bonding, responsible for the strengthening of the M–O_2 bond, is more important in non-dissociable compounds, while the population of the O–O bond in such compounds is smaller than in dissociable compounds, which is consistent with the concept of a greater weakening of the O–O bond in non-dissociable compounds.

The results of ultraviolet spectroscopic studies on the interaction of catalytically active 'onium compounds of the type M_nAX, where A = S, P, Se, or Te and X = Cl, Br, I, BF_4, or ClO_4, with molecular oxygen were used to carry out a semiquantitative calculation by the SCF method[118], from which it follows that (1) not only fully populated *d* orbitals but also only partly populated orbitals can be involved in the activation of molecular oxygen, (2) the electron density of *d* orbitals can serve as a measure of the activation of molecular oxygen, and (3) the *d* orbitals of the catalytic centre can interact with the molecular orbitals located above the $1\pi_g$ orbital.

An X-ray diffraction analysis of an iron complex which is a matrix model of myoglobin has been carried out for the first time[119] (Fig. 8). It showed that the Fe–O–O plane is bisected by the angle between the two adjacent Fe–N bonds in the equatorial plane, which is probably a common feature of both iron and cobalt complexes (Fig. 6).

Resolution of the structure of the Fe–O–O fragment demonstrates the possibility of two statistically equally probable positions of the dioxygen group in mutually perpendicular planes.

Depending on the position of the Fe–O–O plane, the *trans*-ligand plane can be either parallel to the former or at right angles to it. The authors note that a difference between the two extreme positions of the *trans*-ligand plane is possible in principle, but the effect caused by this difference has not so far been discovered. A calculation yielded the following results: d_{O-O} = 1.23 ± 0.08 and 1.26 ± 0.08 Å, the angle Fe–O–O = 135° ± 4° and 137° ± 4°, and d_{Fe-O} = 1.75 ± 0.02 Å. The reduced Fe–O bond length is comparable with the Co–O bond length, which is usually in the range of 1.90 Å.

Among the new dioxygen complexes (matrix models of myoglobin), mention should be made of the paramagnetic complex Fe(αααα-TpivPP)$(THF)_2O_2$ (μ = 2.4 B.M.)[120] where αααα-H_2TpivPP = *meso*-tetra-(αααα-*o*-pivalamidophenyl)porphyrin and THF = tetrahydrofuran. This complex is capable of many repetitions of the deoxygenation–oxygenation cycle in the solid state with concomitant changes in magnetic susceptibility.

The structure of the mononuclear complex $(Et_4N)_3[Co(CN)_5O_2].5H_2O$,[121] in which the Co–O–O angle is 175° ± 2° according to structural studies, i.e. the Co–O–O fragment is nearly linear, is of considerable interest. Unfortunately the authors note that the accuracy of the observed Fe–O–O angles and O–O bond lengths is greatly influenced by the thermal motion of the O_2 group.

The high-spin complex[122] $[Bu_4N][Co(PFP)(HPFP)O_2]$, where Bu_4N is tetrabutylammonium and PFP and HPFP are the dibasic and monobasic residues of perfluoropinacol $[(CF_3)_2C(OH)C(OH)(CF_3)_2]$ occupies a special place. Its magnetic moment is 3.64 ± 0.04 B.M. Studies of its electronic spectra led to the hypothesis that a Co–O_2 bond is formed in this complex without charge transfer.

A copper complex of a polymeric ligand[123], capable of reversible interaction with molecular oxygen and carbon monoxide, was obtained for the first time quite recently[123]. A polyoxime, obtained from an alternant copolymer of ethylene and carbon monoxide, was used as a ligand. Its

unit is described by the formula $\{[CH_2-CH_2]_{1.2}[C]\}$ and its molecular weight is 4000. It is believed that copper is in the monovalent state.

The latest electrochemical studies on dioxygen complexes of cobalt[124] showed that the redox potential of the Co^{II}/Co^{III} system reflects the overall effect of the σ- and π-interactions and steric factors, in conformity with the specific ligand environment.

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Thermodynamics of the Interaction of the Lanthanides with Other Elements

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The thermodynamic characteristics (Gibbs free energies, enthalpies, and entropies) of the interaction of the lanthanides with various elements to form binary compounds and solid or liquid alloys are described. The dissociation energies of gaseous compounds are briefly analysed and experimental and calculated data are compared. The variation of the thermodynamic characteristics of the compounds in the lanthanum-lutetium series is considered from the standpoint of the electronic structures of the components. The thermodynamic behaviour of europium and yttrium in relation to the other lanthanides is discussed.
The bibliography includes 360 references.

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I. INTRODUCTION

The bulk of the thermodynamic data for the lanthanides was obtained in the last two—three decades. The thermodynamic properties of numerous simple and complex lanthanide compounds both in the solid state and in solution were investigated during this period[1-4]. Towards the end of the 1960s refractory lanthanide compounds and alloys began to be studied. The experimental technique of the investigation of such systems is fairly complex and the number of the relevant experimental studies increased slowly. For this reason, the thermodynamic characteristics of many such compounds have been calculated.

The early investigations of the thermodynamic properties of lanthanide compounds are described in Serebrennikov's[5] and Gschneidner's[6] monographs and in Montgomery's review[7]. We shall consider some of these early studies because the data obtained in them have been transferred without due critical analysis from handbook to handbook, owing to the lack of other results, and have served in many publications as "reference" experimental data. During the last 5—7 years, reviews have been published on the thermodynamics of lanthanide halides[8,9] and oxides[10-14], certain refractory compounds of lanthanides with *p* elements[11,15,16], and alloys[17]. Krestov's monograph[3] deals with the thermodynamic characteristics of the lanthanide ions in the gaseous state and in solution, the temperature variation of the properties of certain lanthanide compounds, and the changes which they undergo in ionisation, hydration, dissolution, formation and ionic sublimation reaction.

The aim of the present review was to give a systematic account and to carry out a critical analysis of the experimental data for the thermodynamics of the interaction of the lanthanides with other elements and to compare them with calculated values. Particular attention was devoted to the relation between the thermodynamic characteristics and the electronic structures of the system components.

II. HALIDES

The trichlorides have been most thoroughly investigated among lanthanide halides. Systematic calorimetric studies on crystalline lanthanide trichlorides were carried out by Bommer and Hohmann[18-20]. Their results agree with those of Matignon[21,22], but in both sets of investigations insufficiently pure lanthanides were used. In later studies by Spedding and coworkers[23-25], Montgomery[26,27], Stuve[28-31], and Polyachenok[32] purer lanthanides were employed. Comparison of the enthalpies of formation of lanthanide trichlorides (Table 1) shows that the corresponding values for $EuCl_3$ and $YbCl_3$ are more positive than the enthalpies of formation of the adjacent lanthanide trichlorides. This apparent anomaly has been accounted for theoretically[35,36].

Table 1. Enthalpies of formation of lanthanide trichlorides.

Lanthanide trichloride	$-\Delta H^\circ_{298}$, mole^{-1}	Refs.	Lanthanide trichloride	$-\Delta H^\circ_{298}$, kcal mole^{-1}	Lanthanide trichloride
$LaCl_3$	255.91±0.20	25	$GdCl_3$	240.09±0.30	25
	255.9	33		239.6	33
	256.18±0.28	26	$TbCl_3$	238.33±1.50	30
$CeCl_3$	252.84±0.02	23, 24		238.4	33
	251.5	33	$DyCl_3$	236.6	33
$PrCl_3$	252.09±0.02	25		235	34
	252.0	33	$HoCl_3$	240.29±1.70	30
$NdCl_3$	245.62±0.02	23, 24		237.8	33
	248.97±0.26	28	$ErCl_3$	239.07±0.20	25
	247.4	33		238.0	33
	246.5	32	$TmCl_3$	235.82±0.40	31
$SmCl_3$	244.18±0.41	27		236.3	33
	244.1	33	$YbCl_3$	229.37±0.72	31
$EuCl_3$	218.74±0.65	29		229.4	33
	219.5	33	$LuCl_3$	234.5	33

While the majority of lanthanides in the solid state under standard external conditions have three valence electrons, europium and ytterbium have only two valence electrons under the same conditions[5]. In the trichlorides all the lanthanides are tervalent. The interaction with chlorine entails a change in the number of valence electrons of europium and ytterbium from two to three and the associated rearrangement of the electronic structure:

$$\mathrm{Eu\,[II,\ 4}f^{7}5d^{0}6s^{2}\mathrm{]} \rightarrow \mathrm{Eu\,[III,\ 4}f^{6}5d^{1}6s^{2}\mathrm{]},$$

$$\mathrm{Yb\,[II,\ 4}f^{14}5d^{0}6s^{2}\mathrm{]} \rightarrow \mathrm{Yb\,[III,\ 4}f^{13}5d^{1}6s^{2}\mathrm{]}.$$

It has been established[35,36] that the energy required for the completion of the above processes is 22 kcal mole^{-1} for europium and 9 kcal mole^{-1} for ytterbium. Other lanthanides are not involved in processes of this kind. As a result the Gibb's free energies and enthalpies of formation of $EuCl_3$ and $YbCl_3$ are more positive than the corresponding values for the trichlorides of the adjacent lanthanides.

Latimer[37] calculated the entropy of formation of lanthanide trichlorides by combining their absolute entropies and the entropies of the initial elements. His entropy data[37] and the experimental enthalpies of formation served as a basis for the calculation of the Gibbs free energies of formation of lanthanide trichlorides[7,37]. The Gibbs free energies for the lanthanide trichlorides were also determined by Karapet'yants[38] by the method of comparative calculation. The thermodynamic characteristics of the formation of individual lanthanide trichlorides have also been investigated[39-47].

Some authors[43-46] calculated the thermodynamic functions of formation of liquid lanthanide dichlorides. The enthalpies of formation of crystalline samarium, ytterbium[48,49], europium[50], and neodymium[32] dichlorides have been determined calorimetrically at 298 K as -195.6 ± 1.0, -184.5 ± 1.7, -197.0 ± 1.3, and -163.2 kcal mole^{-1} respectively. These results are consistent with the values calculated for praseodymium, neodymium, samarium, europium, erbium, and ytterbium dichlorides from the fusion diagrams and vapour pressures in systems of the type $Ln-LnCl_3$.[51-56] According to Turnbull and Watts[57] and Valentine et al.[58] the Gibbs free energy of the formation of $PrCl_2$ is -156 kcal mole^{-1} and its enthalpy of formation is -158 kcal mole^{-1} [57] or -167 kcal mole^{-1}.[58] The enthalpies of formation of all the lanthanide dichlorides have been calculated from the Born–Haber cycle[51,59,60]. The enthalpies of formation of the crystalline dichlorides exhibit double periodicity in the series of lanthanides—there are extrema corresponding to $EuCl_2$ and $YbCl_2$ (Fig. 1). The difluorides exhibit a similar relation[59]. The standard enthalpy of formation of EuF_2 evaluated from tensimetric data[61] is -284 ± 17 kcal mole^{-1}.

Experimental enthalpies of formation of lanthanide trifluorides were obtained by Polyachenok[62,63]: -405, -401, -395, -389, and -378 kcal mole^{-1} for LaF_3, PrF_3, NdF_3, GdF_3, and ErF_3 respectively. Their accuracy is to within 5–7 kcal mole^{-1}. The data for the above five trifluorides were also used to estimate by interpolation the enthalpies of formation of the trifluorides of other lanthanides[63]. The enthalpies of formation of trifluorides at 298 K have been determined in a calorimetric study of the precipitation of lanthanide trifluorides from aqueous solutions[64,65] and the following values were obtained (in kcal mole^{-1}): -403.7 ± 1.5 for LaF_3, -402.0 ± 1.5 for CeF_3, -401.5 ± 1.5 for PrF_3, -398.5 ± 0.5 for NdF_3, -398.6 ± 4.0 for SmF_3, -373.8 ± 4.0 for EuF_3, -397.5 ± 0.5 for GdF_3, -388.6 ± 2.0 for ErF_3, and -382.1 ± 2.0 for YbF_3.

The following expressions for the Gibbs free energies of formation of lanthanide trifluorides have been obtained by an e.m.f. method using a solid electrolyte (anionic conductor):

$\Delta G = -(411.38 \pm 0.81) + (57.46 \pm 0.9) \cdot 10^{-3}T \pm 1.4$ kcal/mole LaF_3, (Refs.66,67),

$\Delta G = -405 + 52.71 \cdot 10^{-3}T$ kcal/mole NdF_3, (Ref.68),

$\Delta G = -402 + 50.77 \cdot 10^{-3}T$ kcal/mole GdF_3, (Ref.68),

$\Delta G = -400.5 + 48.42 \cdot 10^{-3}T$ kcal/mole DyF_3, (Ref.68),

$\Delta G = -397.5 + 45.66 \cdot 10^{-3}T$ kcal/mole ErF_3, (Ref.68),

$\Delta G = -394.5 + 44.89 \cdot 10^{-3}T$ kcal/mole β-LuF_3, (Ref.68).

$\Delta G = -387 + 37.08 \cdot 10^{-3}T$ kcal/mole α-LuF_3, (Ref.68).

The enthalpies of formation of lanthanide trifluorides calculated[59] from the Born–Haber cycle are higher by 30–50 kcal mole^{-1} than the experimental values. The data of Brewer et al.[69], which have been used in a number of texts[3,8,70,71], are also higher than the experimental results. On the other hand, the data in the handbook of Wicks and Block[72] are lower than the experimental enthalpies of formation of the trifluorides[62-68,73]. The thermodynamic functions of formation of certain lanthanide fluorides were studied in other investigations also[74-81]. Certain data[4,65,72] reflect the energy of the change in the number of valence electrons of europium[36]. In others this factor[3,34,63,78] is disregarded.

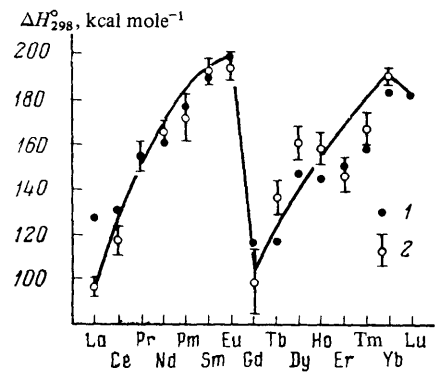

Figure 1. The standard enthalpies of formation of solid lanthanide dichlorides: 1) Novikov and Polyachenok's data[59]; 2) Johnson's data[60].

Estimates of the enthalpies of formation of crystalline lanthanide tribromides have been published[8,47,69,72,79,80]. The data quoted by Wicks and Block[72] are appreciably lower in absolute magnitude than those in other publications. The effect of the change in the number of valence electrons of europium and ytterbium from two to three has been reflected in the enthalpies quoted by Thoma[8], but has been disregarded by other authors[34,78,79]. The thermodynamic functions of europium tribromide[82] and dibromide[83] have been determined experimentally. The enthalpy and Gibbs free energy of formation of $EuBr_3$ at 293.15 K are respectively -186 ± 3.0 and -179.3 ± 3.0 kcal mole^{-1}. For solid $EuBr_2$, $\Delta H^{\circ}_{298} = -178.0 \pm 3.0$ kcal mole^{-1}, $\Delta S^{\circ}_{298} = -16.2 \pm 3.0$ e.u., and $\Delta G^{\circ}_{298} = -173.2 \pm 3.0$ kcal mole^{-1}. Estimates are available for samarium, europium, and ytterbium dibromides[69].

The experimental determinations of the enthalpies of formation of lanthanide tri-iodides[8,20] are inconsistent. The Gibbs free energies have been calculated[37,38]. The data in handbooks[71,72] for the tri-iodides have only been estimated, as in other publications[69,78,84]. The formation of solid EuI_2 at 298.15 K is accompanied by the evolution of -138.0 ± 5 kcal mole^{-1} of heat[85].

The enthalpies of formation and dissociation energies of gaseous lanthanide monohalides, dihalides, and trihalides have been studied[86-97]. According to tensimetric data, the dissociation energies of EuI_2,[95] $EuCl_2$,[95] and $YbCl_2$,[96] are respectively 156.0 ± 5.0, 212.0 ± 2.3, and 193.5 ± 3.2 kcal mole^{-1}. Certain problems of the energetics and stability of gaseous lanthanide halides have been solved by Polyachenok[94] by estimating the thermodynamic quantities using methods of comparative calculation. The atomisation energies of various groups of lanthanide halides in the lanthanum–lutetium series exhibit a double periodicity with minima corresponding to europium and ytterbium. The standard enthalpies of formation of lanthanide monohalides and dihalides show that their stability increases from lanthanum to europium and from gadolinium to ytterbium. The enthalpies of formation of lanthanide trihalides vary monotonically in the series La–Lu with extrema at Eu and Yb. The accuracy of the estimates[94] obtained by methods of comparative calculation is to within ≈10–15 kcal mole^{-1}.

III. CHALCOGENIDES

The principal data for the enthalpies of formation of the oxides were obtained calorimetrically by the combustion of lanthanum[21,98-102], cerium[99,100,103-105] Ce_2O_3,[106,107] neodymium[99,105,108], samarium[105,106,109,110], europium[111,112], gadolinium[113], dysprosium[114,115], holmium[116], erbium[105,117], thulium[118], ytterbium[114], and lutetium[119] in oxygen and by low-temperature calorimetric measurements for the dissolution of the lanthanides and the oxides La_2O_3,[21,26,120,121] Pr_2O_3 (hexagonal)[122,123], Pr_2O_3 (cubic)[123,124], $PrO_{1.833}$,[122,123] PrO_2,[124] $PrO_{1.717}$,[122] $PrO_{1.804}$,[122] Nd_2O_2 (hexagonal)[14], Sm_2O_3,[110] Eu_2O_3,[29,112] $TbO_{1.500}$,[125,126] $TbO_{1.710}$,[125] $TbO_{1.805}$,[125] $TbO_{1.510}$,[126] $TbO_{1.709}$,[126] $TbO_{1.817}$,[126] $TbO_{1.975}$,[126] $TbO_{2.000}$,[126] and Dy_2O_3.[115] The available entropies of the lanthanide oxides have been recently analysed[10,14] by a method for the calculation of entropy based on Latimer's scheme for the resolution of the entropy of a compound into those of its atomic components. The entropies of formation of the latter were calculated by combining the entropies of the lanthanides and their oxides[14]. The enthalpies, Gibbs free energies, and entropies of formation of various lanthanide oxides are compiled in Tables 2 and 3.

Having analysed various high-temperature data for the oxides, Holley et al.[14] tabulated the enthalpies ΔH°_T, entropies ΔS°_T, and Gibbs free energies ΔG°_T of formation of the lanthanide oxides in the temperature range 100–2000 K.

The oxides with a cubic structure have more negative enthalpies of formation than those of the oxides with monoclinic or hexagonal structures. The Gibbs free energies and entropies of formation of europium and ytterbium sesquioxides are lower than the values for the corresponding oxides of the adjacent lanthanides.

The thermodynamic functions of the oxides in the composition range CeO_2–Ce_2O_3 have been investigated[128-131] by an electromotive force method in cells with a solid oxide electrolyte (an anionic conductor). The equilibrium oxygen pressures over cerium oxides were measured in the same composition range[128,132,133] at temperatures from 600° to 1170°C by a dynamic method in an H_2O–H_2 or CO_2–CO gas stream. The thermodynamic properties of the oxides $PrO_{1.5}$–$PrO_{1.714}$ were also studied electrochemically[134]. Data obtained by various experimental methods for solid lanthanide oxides agree satisfactorily with one another.

Table 2. Thermodynamic characteristics of the formation of lanthanide oxides[14,110,112].

Oxide	$-\Delta H^\circ_{298.15}$, kcal mole^{-1}	$-\Delta S^\circ_{298.15}$, e.u.	$-\Delta G^\circ_{298.15}$ kcal mole^{-1}
La_2O_3 (hexag.)	428.7±0.18	70.04±0.45	407.82±0.23
CeO_2	260.6±0.2	52.24±0.18	245.0±0.3
Ce_2O_3 (hexag.)	430.9±3.8	73.5±0.62	409.0±3.8
Pr_2O_3 (hexag.)	435.8±1.6	70.5±1.0	414.8±1.6
$PrO_{1.833}$	227.6±0.8	43.5±0.5	214.7±0.8
Nd_2O_3 (hexag.)	432.37±0.21	72.12±0.46	411.17±0.25
Sm_2O_3 (monocl.)	435.86±0.45	70.65±0.35	414.8±0.5
Sm_2O_3 (cubic)	436.76		
Eu_2O_3 (monocl.)	394.7±0.8	76.0±2.0	372.0±0.9
Eu_2O_3 (cubic)	397.7±0.9		
Gd_2O_3 (monocl.)	433.94±0.87	68.3±1.7	413.4±1.0
Tb_2O_3 (cubic)	445.6±1.8	71.0±1.0	424.4±1.8
$TbO_{1.709}$	227.4±0.9	40.3±0.5	215.4±0.9
Dy_2O_3 (cubic)	445.19±0.85	66.10±0.27	425.5±0.9
Ho_2O_3 (cubic)	449.5±1.15	71.9±0.55	428.1±1.15
Er_2O_3 (cubic)	453.59±0.45	71.86±0.41	432.16±0.47
Tm_2O_3 (cubic)	451.4±1.4	72.4±1.0	428.8±1.4
Yb_2O_3 (cubic)	433.68±0.53	70.32±0.30	412.71±0.54
Lu_2O_3 (cubic)	448.9±1.8	71.9±1.0	427.5±1.8

The enthalpy of formation of crystalline $EuO_{1.02}$ was determined calorimetrically[135] at 298 K as -145.2 ± 2.8 kcal mole^{-1}. The Gibbs free energies of formation of EuO, YbO, and SmO are respectively −10, 7, and 13 kcal mole^{-1}.[136]

Table 3. Enthalpies of formation of cerium, praseodymium, and terbium oxides[122-127].

Oxide	$-\Delta H^\circ_{298.15}$, kcal mole^{-1}	Oxide	$-\Delta H^\circ_{298.15}$, kcal mole^{-1}	Oxide	$-\Delta H^\circ_{298.15}$, kcal mole^{-1}
Ce_2O_3 (hexag.)	435.0	Pr_2O_3 (hexag.)	435.8±1.6	Tb_2O_3	445.6±1.8
$CeO_{1.67}$ (cubic)	233	Pr_2O_3 (cubic)	436.8±1.6	$TbO_{1.709}$	227.4±0.9
$CeO_{1.72}$ (orthorhomb.)	238	$PrO_{1.717}$	224.0±0.9	$TbO_{1.817}$	229.7±0.9
$CeO_{1.78}$ (orthorhomb.)	244	$PrO_{1.804}$	226.5±0.8	$TbO_{2.000}$	232.0±0.7
$CeO_{1.81}$ (orthorhomb.)	247	$PrO_{1.833}$	225.2±0.2	—	—
CeO_2 [110]	260.6	$PrO_{1.833}$	227.6±0.8	—	—
—	—	$PrO_{2.000}$	232.9±1.5	—	—

Although rough estimates of the dissociation energies D°_0 of gaseous lanthanide monoxides had been obtained in earlier studies[137-139], the first accurate values of D°_0 were apparently obtained for LaO,[140-143] NdO,[141-143] SmO,[141-143] GdO,[142,143] TbO,[143] and LuO[142,143] by the mass-spectrometric method in combination with Knudsen's method. These characteristics were investigated in greatest detail by Ames[144,145]. Subsequent studies[146-150] yielded similar results. The dissociation energy of LaO was found to be 192.5,[140] 187.0 ± 4.6,[141] 186.4 ± 4.6,[142] 190.5 ± 4.6,[143] 193.5,[145] 192.5,[146] 189.5,[148] 190.3 ± 1.0,[147]

and 189.9 ± 1.0 [148] kcal mole^{-1}. The following dissociation energies have been obtained for other lanthanide monoxides (in kcal mole^{-1}): 190.5,[143] 193.5,[145] 185.2,[151] and 188.6 [152] for CeO, 175.8,[143] 182,[145] and 171.0 ± 6.9 [151] for PrO, 171.0 ± 4.6,[141] 163.4 ± 4.9,[142] 168.1 (169),[143] 172.1 (174.5),[145] 163.0,[151] and 170.3 [16] for NdO, 142.7 [143] and 142.4 ± 4 [145] for SmO, 133.3,[143] 134.7 ± 1.3,[145] and 133.9 [153] for EuO, 162.0 ± 6.9 [143] and 173 ± 3 [145] for GdO, 170.3 [143] and 173.8 [145] for TbO, 150.4 ± 0.6 for DyO,[145] 152.7 ± 2.0 for HoO,[145] 151.6 ± 0.8 for ErO,[145] 139.2 ± 0.7 for TmO,[145] 88.4 ± 0.8 for YbO,[145] and 159.5 ± 6.9 [143] and 167 ± 3 [145] for LuO. The corresponding enthalpies of formation of the gaseous monoxides are also quoted in the above studies. Gordienko et al.[16] recommend the following values of ΔH_0° (kcal mole^{-1}):

LaO	CeO	PrO	NdO	SmO	EuO	GdO	TbO	DyO	HoO
31.3	22.3	33.3	36.2	34.5	32.7	17.8	20.0	20.1	23.8
ErO	TmO	YbO	LuO						
17.1	20.8	—7.2	5.5						

Table 4. Enthalpies of formation of solid lanthanide monosulphides and dissociation energies of the gaseous monosulphides at 298 K.

Lanthanide monosulphide	$-\Delta H_{298}^\circ$, kcal mole^{-1}	References	D_{298}°, kcal mole^{-1}	References
LaS	113±1	156, 157	141.3±4.9	159
	113.3	159–161	138.8±6	159
	110.5	159	145.3	161
	108±4	162		
CeS	112±1	156	—	—
	118±2	154		
	109±1	7		
PrS	111±1	156	118.3	159, 163, 164
	109	16, 164, 170	117.7±1.1	170
NdS	111±1	156	113	159, 164
	104.8	161	118.1	161
	108.5	16, 164		
SmS	103.2	170	93	170
EuS	97.5	16, 170	—	—
	106.7±1.3	166		
GdS	105±1	156	109.5	161
	78.5	161		
YbS	97.9	170		

The thermodynamic characteristics of lanthanide sulphides were apparently obtained for the first time by Matignon[22] and Biltz[102]. Subsequently these investigations were assessed critically[154–156] using for the calculation of the enthalpies of formation of the solid sulphides the heats of solution of the lanthanides quoted in other reports[23–25]. After recalculation, the relevant values were found to be close to the enthalpies of formation of the sulphides based on data derived from systematic calorimetric studies[156–158]. The enthalpies of formation of the sulphides and the dissociation energies of the gaseous lanthanide monosulphides are quoted in Table 4. The studies were carried out mass-spectrometrically[159–166]. The enthalpies of formation of solid sulphides of different compositions are compiled in Table 5. The entropies and Gibbs free energies of formation of lanthanide sulphides have been estimated[7,37,76,167] and the high-temperature thermodynamic characteristics of solid lanthanide monosulphides have been tabulated[16,163,164,168,169].

Table 5. Enthalpies of formation of lanthanide sulphides at 298 K (kcal mole^{-1}).

Lanthanide	Ln_2S_3		Ln_3S_4		LnS_2	
	$-\Delta H_{298}^\circ$	references	$-\Delta H_{298}^\circ$	references	$-\Delta H_{298}^\circ$	references
La	282±3	156	401.4	157	144.4	157
	282±10	155	—	—	149±8	7
	192±16	7	—	—	—	—
Ce	277±3	156	392.0	157	142.2	157
	300±8	154	394.8	7	146.3±2.0	7
	282±2	7	—	—	—	—
Pr	273±3	156	391.0	157	141.0	147
Nd	269±3	156	388.0	157	138.8	147
	285.9	22				
	277	7				

The dissociation energies of the gaseous sulphides were determined mass-spectrometrically[170–175]. The variation of the dissociation energies of the gaseous monosulphides, monoxides, monoselenides[176,177], and monotellurides[176] in the La–Lu series is illustrated in Fig. 2. The dissociation energies[161,178] of PrSe, NdSe, and SmSe are much higher[176]. The standard enthalpies of formation of LaSe, PrSe, NdSe, SmSe, and EuSe calculated from mass-spectrometric data are −82, −123.5, −151.5, −147.0, and −107.5 kcal mole^{-1} respectively. The considerable difference between the enthalpies of formation of SmSe and EuSe is unexpected, because samarium and europium in the monoselenides are both bivalent[179].

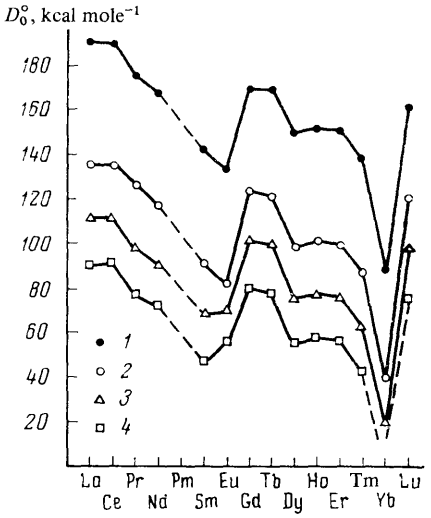

Figure 2. Variation of the dissociation energies of the monochalcogenides in the series of lanthanides: 1) monoxides; 2) monosulphides; 3) monoselenides; 4) monotellurides[176].

The enthalpies of formation of Gd_2Se_3 (−255.3 ± 8.1 kcal mole^{-1}),[180] Gd_2Te_3 (−221.4 ± 5.3 kcal mole^{-1}),[180] and La_2Te_3 (−187.5 ± 6.1 kcal mole^{-1})[181] were determined calorimetrically. The Gibbs free energies, enthalpies, and

entropies of formation of the higher lanthanum tellurides were calculated from e.m.f. data[182]:

	$-\Delta G_{880°K}$, kcal g-atom^{-1}	$-\Delta H$, kcal g-atom^{-1}	$-\Delta S$, e.u.
$La_{0,25}Te_{0,75}$	27.30±0.01	28.26 ± 0.16	1.42 ± 0.22
$La_{0,286}Te_{0,714}$	31.30±0.01	32.30±0.15	1.62±0.20

IV. PNICTIDES

The enthalpy of formation of LaN is lower[183-186] than that of CeN (Table 6) in which cerium is partly present in the quadrivalent state[6]. In the series of lanthanide arsenides[187] the enthalpy of formation of YbAs has the highest (least negative) value in consequence of the expenditure of energy in the change of the number of valence electrons of ytterbium from two to three[36]. The enthalpies of formation of the monoarsenides have been determined by differential calorimetry within wide confidence limits. The intermediate compounds in the lanthanum–antimony system and gadolinium antimonide have high enthalpies of formation and negative entropies of formation in the temperature range 653–803 K investigated by an e.m.f. method[188-191] (Table 7). The heats of atomisation of praseodymium monopnictides decrease from arsenic to bismuth[192].

Table 6. Enthalpies of formation of lanthanide mononitrides[183-186] and monoarsenides[187].

Compound	$-\Delta H°$, kcal mole^{-1}	Compound	$-\Delta H°$, kcal mole^{-1}
LaN	72±3	GdAs	74.4±3.2
CeN	78±3	TbAs	75.0±3.4
LaAs	73.0±4.5	DyAs	78.1±5.0
CeAs	68.9±3.0	HoAs	72.3±3.3
PrAs	73.4±3.1	ErAs	75.6±3.2
NdAs	72.7±3.5	TmAs	72.8±3.2
SmAs	72.0±3.5	YbAs	61.8±2.9
		LuAs	75.6±3.1

Table 7. Thermodynamic characteristics of the formation of lanthanum and gadolinium antimonides[188-191].

Phase	$-\Delta H$, kcal g-atom^{-1}	$-\Delta S°$, e.u.	$-\Delta G°_{730°K}$, kcal g-atom^{-1}
$LaSb_2$	23.25±0.19	1.28±0.26	22.32±0.01
$La_{0,53}Sb_{0,47}$	35.42±0.44	2.94±0.65	33.25±0.01
La_4Sb_3	35.58±0.51	2.81±0.74	33.53±0.01
La_5Sb_3	35.34±0.65	3.07±0.83	33.14±0.01
La_2Sb	33.96±0.87	3.53±1.23	31.36±0.02
$Gd_{0,52}Sb_{0,48}$	32.77±0.60	1.80±0.79	31.46±0.01

V. CARBIDES, SILICIDES, AND BORIDES

The main studies on the thermodynamics of the formation of lanthanide dicarbides have been carried out mass-spectrometrically in combination with Knudsen's tensimetric method[193-223]. The dissociation energies of the gaseous dicarbides and the heats of evaporation, atomisation, and formation of solid dicarbides were calculated in these investigations using the Second and Third Laws of thermodynamics. The thermodynamic characteristics of formation of a number of dicarbides and sesquicarbides have been studied by an e.m.f. method[224,225] and calorimetrically[105]. The enthalpies of formation of the lanthanide dicarbides calculated from the results of different investigations agree provided that the Third Law was used in the calculations. The standard enthalpies of formation of lanthanide dicarbides calculated from e.m.f. data using the Second Law differ appreciably from tensimetric data[225].

Table 8. Standard enthalpies of formation of lanthanide dicarbides.

Lanthanide dicarbide	$-\Delta H°_{298}$, kcal mole^{-1}	References	Lanthanide dicarbide	$-\Delta H°_{298}$, kcal mole^{-1}	References
LaC_2	19	199	EuC_2	16.1±1.0	200
	21	195		9.17±1.15	205
	21.3	203		16.0±1.3	204
	20.9	225		30.6	197
CeC_2	25	199	GdC_2	30±9	196, 198
	17	201		24.2	225
	19.5	201			
	15±5	213	DyC_2	11±1	214
	21.2	225		22.5	225
	23.2±1.3	105	HoC_2	19.8	212
PrC_2	20.2	225		21±1	214
				19.83	226
NdC_2	12.5	199	ErC_2	18.5±0.4	215
	21.2	225		26.5	225
SmC_2	15.6±1.6	199	YbC_2	18.0±1.0	206
	15.2±2.0	200	LuC_2	18±5	220
	18.4±1.3	207			
	23.4±2.0	208			

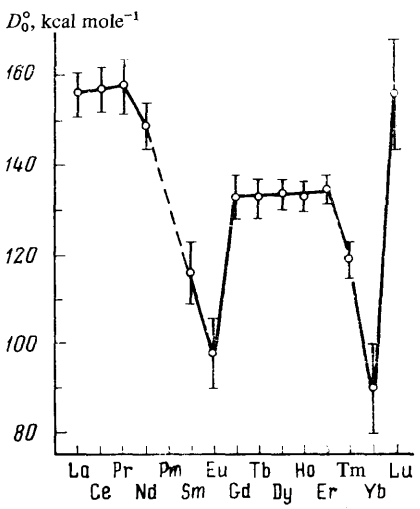

Figure 3. Variation of the Ln–C_2 bond energy in the series of lanthanides[218-220].

The enthalpies of formation of various lanthanide dicarbides are compiled in Table 8. They vary about 20 kcal mole^{-1}. The variation of the Ln–C_2 bond energy in the series of gaseous lanthanide dicarbides exhibits double periodicity (Fig. 3).

The Gibbs free energies of formation of lanthanum, cerium, praseodymium, and neodymium sesquicarbides from the liquid lanthanides and solid graphite, determined by an e.m.f. method[224], are higher than the values calculated for Ce_2C_3 from the phase diagram[227]. The enthalpy of formation of $CeC_{1.5}$ was found to be -21.1 ± 0.7 kcal mole^{-1} at 298.15 K by combustion in a bomb calorimeter[105]. The standard enthalpy and entropy of formation of Ho_2C_3 are -11.1 kcal mole^{-1} and 5.1 e.u. respectively according to tensimetric data[226].

The thermodynamic studies on the silicides are apparently limited to LaSi, β-$LaSi_2$, and β-$CeSi_2$, whose enthalpies of formation are respectively -30.0,[228] -44.4,[228] and -50 [229] or -45 [230] kcal mole^{-1}.

The first enthalpies of formation of lanthanum, cerium, and yttrium borides were obtained in Refs. 231–237. They were used to calculate by the thermochemical logarithmic rule the enthalpies of formation of the hexaborides of the entire series of lanthanides[234,235]. However, the monotonic increase of the modulus of this quantity in the series from lanthanum to lutetium is unlikely.

The heats of dissociation of the gaseous hexaborides and the enthalpies of formation of the solid compounds have been determined from mass-spectrometric measurements[236-242] by the method of Langmuir and Knudsen. The heats of dissociation decrease steadily from LaB_6 to SmB_6 (Table 9). A similar variation has been observed also for lanthanide diborides[243].

Table 9. Enthalpies of dissociation and formation of lanthanide hexaborides[241,242].

Lanthanide hexaboride	Temp. range, K	Enthalpy of dissociation, kcal mole^{-1}	Enthalpy of formation, kcal mole^{-1}
LaB_6	2045–2300	134.2±2.7	−28±4
CeB_6	1846–2220	123.1±2.8	−11±4
PrB_6	1943–2200	111.5±2.5	−23.5±4
NdB_6	1983–2300	107.9±2.2	−29.5±3
SmB_6	2050–2370	102.8±2.3	−54±3
GdB_6	2170–2500	127.0±2.8	−31±4
TbB_6	1980–2350	128.7±3.4	−34±5

VI. HYDRIDES

The thermodynamic characteristics of the formation of the dihydrides of the majority of lanthanides and also of some of their dideuterides have been calculated from the temperature variation of the pressure of hydrogen formed on dissociation of these compounds (Table 10).[244-256] On passing from the hydrides to the deuterides, the thermodynamic functions of formation diminish. Gschneidner reported[257] that the enthalpies of formation of terbium, dysprosium, thulium, and lutetium dihydrides are close to the enthalpies of formation of the dihydrides of the adjacent lanthanides. The equilibrium pressure and partial thermodynamic characteristics of hydrogen were also studied for lanthanum[258,259] and gadoliunium[260] dihydrides. The enthalpies of dissociation of the higher non-stoichiometric lanthanide hydrides to the dihydrides have been calculated[261-263] as 10–20 kcal/mole H_2. There has been only one calorimetric study[264] on $LaH_{2.8}$, $CeH_{2.7}$, and $PrH_{2.7}$.

VII. METALLIC ALLOYS WITH *p* ELEMENTS

The first studies[265-267] carried out by an e.m.f. method using a liquid electrolyte (a cationic conductor) already demonstrated a marked interaction of the lanthanides with bismuth and lead. The results of studies up to 1969 on the thermodynamics of lanthanide alloys have already been reviewed[17]. The intermediate phases in the cerium–lead, praseodymium–lead, and neodymium–lead systems were investigated[268] by a modified Knudsen method.

Table 10. Enthalpies and entropies of formation of lanthanide dihydrides.

Lanthanide dihydride	$-\Delta H^\circ_{298}$, kcal/mole H_2	$-\Delta S^\circ_{298}$, e.u.	Refs.	Lanthanide dihydride	$-\Delta H^\circ_{298}$, kcal/mole H_2	$-\Delta S^\circ_{298}$, e.u.	Refs.
LaH_2	49.6±1.0	35.5±1.0	244	GdH_2	45.2±0.1	43.1±0.1	248
LaD_2	46.5±1.0	33.1±1.0	244	GdH_3	46.9±0.7	—	249
LaH_2	49.7±0.1	—	245	HoH_3	52.7	35.6	250
CeH_2	49.2±1.0	35.4±1.0	244	HoD_3	52.3	35.8	250
CeD_2	46.3±1.0	33.5±1.0	244	ErH_2	53.5	36.5	247
CeH_2	33.9±0.9	—	245	ErH_2	52.6±0.3	35.2±0.3	251
CeH_3	48.3	34.1	246	ErH_3	48.3	32.3	252
PrH_2	49.7±1.0	35.0±1.0	244	ErH_2	55.2	51.1	253
PrH_2	47.8	—	245	ErD_2	52.2	48.6	253
NdH_2	50.5±1.0	34.8±1.0	244	ErD_2	53.0±0.2	36.3±0.2	254
NdH_2	44.8	—	245	YbH_2	43.3	33.4	255
SmH_2	53.3	—	247	YbH_2	42.9±1.2	29.2±1.7	256
SmH_2	43.0±0.5	39.4±0.2	248				

E.m.f. studies on the cerium–lead system[269] yielded appreciably different thermodynamic characteristics of formation of $CePb_3$, particularly as regards the Gibbs free energy. The ytterbium–aluminium system was studied tensimetrically over a wide range of compositions and the equation $\Delta G^\circ_T = -17\,473.16 + 9.405\,T$ (cal mole^{-1}) was fitted to the Gibbs free energies of formation of $YbAl_2$ in the range 773–873 K.[270] The alloys of lanthanides with aluminium gallium, indium, thallium, tin, lead, and bismuth were studied mainly in the range of compositions with a high content of the non-lanthanide metal. The thermodynamic characteristics of formation of compounds of the lanthanides with the above *p* elements found by an e.m.f. method and the equations for the temperature variation of the activity coefficients of the lanthanides in the liquid alloys are presented in Table 11. When a galvanic cell of the amalgam type is used in the study of the thermodynamic properties of lanthanide–aluminium alloys, it is necessary to take into account the displacement of the lanthanide ion from the electrolyte by aluminium. This factor was neglected in a number of the investigations[271,272,297,298], which probably accounts for certain discrepancies between the data of Kober et al.[272] and Degtyar' et al.[299], the latter having been obtained by a method based on the distribution in the system aluminium–lanthanum–bismuth. Calorimetric studies on the enthalpies of mixing of the lanthanides with aluminium were begun recently[297,298,300]. Palenzona and Cirafici[301] determined the enthalpies of formation of thirteen compounds of lanthanides and lead of the type $LnPb_3$ by dynamic differential calorimetry. Ferris et al.[302] calculated with a low accuracy the activity coefficients of lanthanum, cerium, neodymium, gadolinium, and dysprosium in liquid, bismuth-based alloys. Smith[303] estimated the heat of solution of samarium in lead as 15 kcal g-atom^{-1}.

The enthalpies of formation of $LaSn_3$ found by an e.m.f. method[288], high-temperature calorimetry of the dissolution process[304,305], and dynamic differential calorimetry[306] agree with one another. The enthalpies of formation of lanthanide–tin compounds of the type $LnSn_3$ and the relative partial molar enthalpies of solution of the lanthanides in tin are compiled in Table 12.

Table 11. Thermodynamic characteristics of the formation of compounds in liquid mixtures of lanthanides and *p* elements.

Compound	$-\Delta H^\circ_T$, kcal mole^{-1}	$-\Delta S^\circ_T$, e.u.	$-\Delta G^\circ_T$ kcal mole^{-1}	T, °K	Coefficients of the equation $\lg\gamma = a - bT^{-1}$		Temp. range, K	Refs.
					a	b		
1	2	3	4	5	6	7	8	9
$LaAl_4$	57.7±0.5	19.6±0.4	38.2±0.1	1000	2.973	9 872	953—1123	271
$CeAl_4$	52.0±0.7	12.2±0.7	42.1±0.1	900	—	—	—	272
$CeAl_4$	63.0±1.3	24.2±1.3	38.8±0.1	1000	3.384	10 530		272
$LaGa_2$	68.6	15.5	53.5	975	5.134	13 853	675—975	273,274
$CeGa_2$	73.2	26.3	47.6	975	7.568	15 173	675—975	275
	—	—	—	—	5.745	13 445	673—973	276
$PrGa_2$	69.4	18.7	51.2	975	5.781	14 091	675—975	277
$NdGa_2$	70.5	19.6	51.4	975	6.024	14 200	675—975	278
$GdGa_2$	(82)	(48)	35.2	975	10.50	15 908	675—975	279
$DyGa_2$	98	66	31	973	7.65	15 078	675—975	280
$ErGa_2$	68	36	33	973	—	—		281
$TmGa_3$	50	23.7	29	873	—	—		282
$LaIn_3$	51.3	10.5	41.1	975	3.170	10 023	725—975	283
$CeIn_3$	57.6	21.1	37.1	975	5.780	11 868	725—975	284
$PrIn_3$	55.3	15.5	40.2	975	3.793	10 531	725—975	285
$NdIn_3$	55.9	17.0	39.3	975	4.186	10 806	725—975	286
$GdIn_3$	47.2±1.2	12.3±1.6	40.1±0.1	773	—	—	673—875	287
$ErIn_3$	40.4±2.4	9.7±3.1	33.0±0.2	773	—	—	673—875	287
$LaTl_3$	45.3	11.0	34.6	975	2.784	8 679	775—975	283
$LaSn_3$	62.7	8.2	54.7	975	4.70	13 900	673—973	288
$NdSn_3$	62.1±0.8	12.9±0.9	49.6±0.1	973	—	—	773—973	289
$GdSn_3$	53.2±2.0	10.3±2.3	42.2±0.2	973	—	—	773—973	290
$LaPb_3$	55.4±1.1	14.2±1.1	41.2±0.2	1000	−0.068	6 618	950—1120	271
$CePb_3$	57.6±0.4	17.4±0.5	39.2±0.1	1000	1.744	8 220	700—1033	269
$NdPb_3$	47.1±0.6	5.2±0.7	42.5±0.2	873	—	—	796—873	291
$GdPb_3$	33.1±0.3	2.26±0.3	31.3±0.1	873	—	—	773—879	292
$ErPb_3$	31.9±0.2	3.8±0.2	28.6±0.1	873	—	—	773—873	293
$LaBi_x$	66.1±0.3	15.1±0.3	52.5±0.1	900	0.844	11 070	753—953	294
$CeBi_x$	64.9±0.5	15.2±0.6	51.2±0.1	900	2.03	11 400	773—923	295,296

Table 12. Enthalpies of formation of compounds of the type $LnSn_3$ and enthalpies of solution of the lanthanides in liquid tin-based alloys.

Lanthanide	$-\Delta H_{LnSn_3}$, kcal mole^{-1}	Temp., K	References	$-\Delta\bar{H}_{Ln(Sn)}$, kcal g-atom^{-1}	Temp., K	References
La	62.7±1.8	773—973	288	61.5±2.0	773—973	288
La	60.6±0.8	273	304	64.4—66.7	725—775	304
La	65.18 (60.25) *	510	306	66.2±0.6	632	305
Ce	54.01 (49.08)	510	306	68.4±0.4	634	305,307
Pr	60.87 (55.94)	520	306	61.3±0.4	750	305
Pr	—	—	—	70.0±2.5	750	308
Nd	70.89 (65.96)	620	306	58±2	750	308
Nd	57.1±0.8	773—973	289	57.1±1.4	773—973	289
Sm	58.48 (53.55)	570	306	53±2	750	308
Sm	53.8	295	309,310	—	—	—
Eu	50.48±1.85	295.7	311	$40.4+167\ C^{**}_{Eu}$	958	311
Gd	49.65±1.65	299.7	312	$41.9+225C_{Gd}$	969	312
Gd	53.72 (48.78)	600	306	—	—	—
Gd	48.2±2.0	773—973	290	51.4±2.6	773—973	290
Dy	—	—	—	$36.44-34.4C_{Dy}$	957	313
Er	—	—	—	$29.25+1.2C_{Er}$	963	313
Yb	50.80 (45.86)	540	306	35.2±0.3	770	305
Yb	42.1	294	314	35.3	857	314
Lu	37.4±0.8***	800	315	—	—	—

* The values of ΔH_{LnSn_3} at 298 K are indicated in brackets.

** c_{Ln} = at.% of the lanthanide.

*** $\Delta\bar{H}_{Ln}$.

It has been established on the basis of the magnetic properties of $EuSn_3$, $YbSn_3$, $EuPb_3$ and $YbPb_3$ that europium and ytterbium in these compounds are bivalent[316,317]. The enthalpies of formation of $EuSn_3$ and $YbSn_3$ (Table 12) are close to the values which can be obtained by interpolation from the enthalpies of formation of compounds of the type $LnSn_3$ of the adjacent tervalent lanthanides. The lanthanide–lead compounds of the type $LnPb_3$ exhibit a similar behaviour[301].

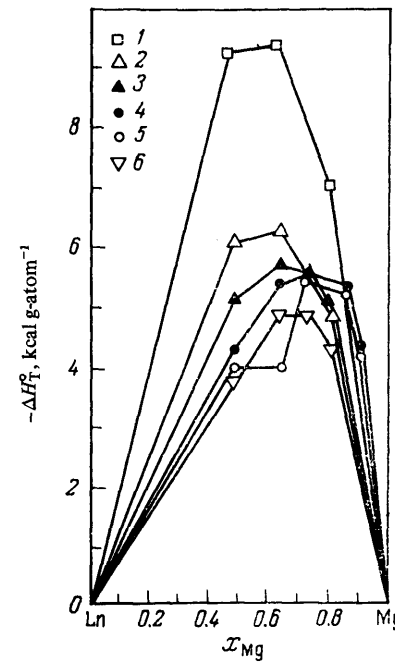

Figure 4. Enthalpies of formation of the intermediate compounds in different systems[318]: 1) Lu–Mg; 2) Er–Mg; 3) Gd–Mg; 4) Nd–Mg; 5) Ce–Mg; 6) Dy–Mg.

VIII. ALLOYS OF LANTHANIDES WITH *s* AND *d* ELEMENTS

The magnesium alloys have been most thoroughly investigated in this group. The intermediate compounds in systems formed by magnesium with cerium, neodymium, gadolinium, dysprosium, erbium, and lutetium have been studied by Knudsen's method[318]. The maximum in the thermodynamic characteristics of formation shift from the composition $CeMg_3$ to $GdMg_2$ and then to LuMg (Figs. 4 and 5). In liquid lanthanum–magnesium melts[319] the maximum Gibbs free energy of mixing of the components is also displaced towards $LaMg_3$. The Gibbs free energies of formation of 12 compounds having the composition LnMg (except for europium and ytterbium) have been studied in the temperature range 700–800 K.[320] The results of two studies[318,320] for the heavy lanthanides differ appreciably. The partial thermodynamic characteristics of cerium in magnesium-based solutions have been calculated at 1083 K: $\Delta\bar{H}^\infty_{Ce} = -26.8$ kcal g-atom^{-1},[321] $\Delta\bar{S}^{exc\,\infty}_{Ce} = -9.8$ e.u.,[321] and $\Delta\bar{G}^{exc\,\infty}_{Ce} = -16.4$ [321] or -15.5 [322] kcal g-atom^{-1}. The partial thermodynamic characteristics

of magnesium have been determined for neodymium–magnesium and samarium–magnesium alloys[323]. The authors[324] explain the negative enthalpy of solution of cerium in sodium by the influence of impurities.

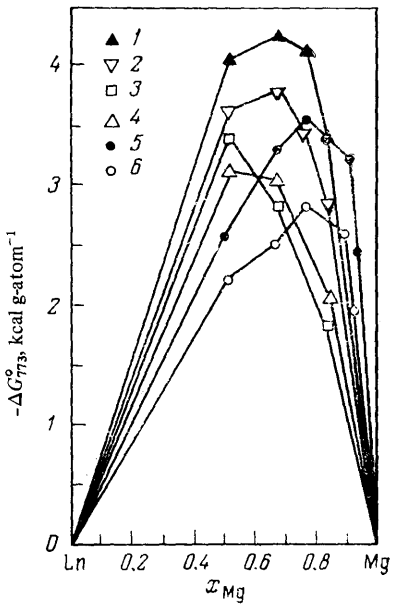

Figure 5. Gibbs free energies of formation of the intermediate compounds at 773 K in different systems[318]: 1) Gd–Mg; 2) Dy–Mg; 3) Lu–Mg; 4) Er–Mg; 5) Nd–Mg; 6) Ce–Mg.

The fairly high volatility of zinc and its remoteness in the electrochemical series from the lanthanides made it possible to investigate lanthanide–zinc alloys by Knudsen's tensimetric method[325-328] and by e.m.f. methods[329-333]. The solid intermediate compounds have been studied in the systems cerium–zinc[325], samarium–zinc[326], praseodymium–zinc[327], and neodymium–zinc[328] and in some of the investigations[325,327] the liquid alloys were also studied. Chiotti[334] showed, using a new method for the integration of the Gibbs–Duhem equation, that some of his earlier results[327] were incorrect. The thermodynamic characteristics obtained by Chiotti and Mason[325,326] were analysed by the present authors in an earlier publication[17].

Alloys of lanthanum, cerium, and praseodymium with zinc and cadmium (Table 13) have been studied by an e.m.f. method[329-333]. The behaviour of lanthanum, cerium, and praseodymium in liquid zinc- and cadmium-based alloys is consistent with Henry's Law. The enthalpies of formation of $NdZn_{11}$, $NdCd_{11}$, and $SmCd_{11}$ have also been estimated[333] by a method of comparative calculation as -86.16, -69.65, and -68.34 kcal mole^{-1} respectively. The Gibbs free energies of formation of compounds of the type LnCd vary about -7 kcal g-atom^{-1} as a function of the atomic number of the lanthanide[320]. The results of thermodynamic studies on the samarium–mercury system by tensimetric[335] and e.m.f. [336] methods do not agree, particularly as regards the enthalpies and entropies (these differ in sign). The interpretation of the e.m.f. of the cell

$$Sm\,|\,Sm(ClO_4)_3 + LiClO_4 + \text{dimethylformamide}\,|\,Sm(Hg)$$

requires further consideration.

Table 13. Thermodynamic characteristics of the formation of lanthanide–zinc and lanthanide–cadmium compounds of the type LnM_{11}.

Compound	$-\Delta H^{\circ}_T$, kcal mole^{-1}	$-\Delta S^{\circ}_T$, e.u.	$-\Delta G^{\circ}_{723°K}$, kcal mole^{-1}	Temp. range, K	References
$LaZn_{11}$	97.4	53.3	56.2		329
$LaZn_{11}$	93.6±0.2	49.1±0.2	55.6±0.1	715—1022	330,332
$LaZn_{11}$	92.58±0.18	48.02±0.24	57.85±0.02	705—793	333
$CeZn_{11}$	86.3±0.6	42.9±0.9	53.1±0.4	723—1020	331,332
$CeZn_{11}$	87.85±0.18	44.98±0.21	55.31±0.09	710—1018	333
$CeZn_{11}$	92.32	46.7	58.56		325
$PrZn_{11}$	85.26±0.19	42.65±0.25	54.42±0.04	696—875	333
$PrZn_{11}$	89.35	45.48	56.47		327
$NdZn_{11}$	91.93	50.56	55.50		328
$LaCd_{11}$	72.34±0.17	48.58±0.22	40.83±0.03	670—804	333
$CeCd_{11}$	70.52±0.15	44.57±0.21	38.29±0.03	638—884	333
$PrCd_{11}$	69.07±0.23	44.82±0.31	36.26±0.06	635—825	333

The thermodynamic characteristics of $LaIr_2$ [337,338] and of the intermediate compounds in the cerium–iridium system[338,339] have been determined by an e.m.f. method using a solid electrolyte (an anionic conductor). The Gibbs free energies of formation (in kcal mole^{-1}) of $LaIr_2$ and $CeIr_2$ in the temperature range 950—1200 K are described by the equations

$$\Delta G^{\circ}_{LaIr_2}(\pm 0.45) = -(44.0 \pm 2) + (1.13 \pm 2)\cdot 10^{-3}T,$$

$$\Delta G^{\circ}_{CeIr_2}(\pm 4) = -(62.5 \pm 4) + (0.10 \pm 3.3)\cdot 10^{-3}T.$$

The thermodynamic characteristics of $CeIr_3$, $CeIr_5$, and Ce_2Ir_7 differ little from those of $CeIr_2$.

Gingerich and coworkers[340-342] demonstrated the high stability of the gaseous monaurides. Their dissociation energies are as follows (in kcal mole^{-1}): 79.5 ± 5.0 for LaAu, 75.5 ± 3.5 for CeAu, 73.0 ± 5.0 for PrAu, 69.5 ± 6.0 for NdAu, 66.8 for TbAu, 60 ± 3 for HoAu, and 78.5 for LuAu. The dissociation energy of HoAg (28.6 ± 4 kcal mole^{-1}) is lower than that of HoAu (59.7 ± 3 kcal mole^{-1})[341]. The atomisation energies of lutetium, holmium, and terbium diaurides have been calculated[342]. The calculation of the bond energies in lanthanide monaurides and diaurides using Pauling's model of a single polar bond yielded results in good agreement with experiment. The dissociation energies of EuAg have been determined experimentally (31.0 ± 3.0 kcal mole^{-1}) and calculated theoretically on the basis of Pauling's model (33.4 kcal mole^{-1})[343].

IX. GENERAL CHARACTERISTICS

The present author calculated the energies of mutual exchange between 14 lanthanides and various elements for 1078 systems from the properties of the initial components by the Hildebrand–Mott method[344]. The most positive energies were found for the mutual exchange between the majority of lanthanides (with the exception of europium and ytterbium) and s^1 elements. Negative values are characteristic of the energies of mutual exchange between

all the lanthanides and *p* elements. Compared with other lanthanides, the energies are higher for the mutual exchange between europium and ytterbium and d^5 elements and lower for the mutual exchange with *s* elements.

The Gibbs free energies and enthalpies of formation of europium and ytterbium compounds are consistent with the general variation of these characteristics for compounds of the type $LnSn_3$ (Table 12) and $LnPb_3$,[301] monosulphides (Table 4), and dicarbides (Table 8) in the series of lanthanides. The Gibbs free energies and enthalpies of formation of the sesquioxides (Table 2), monoarsenides (Table 6), trichlorides (Table 1), and trifluorides are more positive for the europium and ytterbium compounds than for the compounds of the adjoining lanthanides. According to the present author's data[345,346] the interaction of calcium and cadmium with europium and ytterbium is more favourable on energy grounds than the interaction with the adjacent lanthanides. These features of the thermodynamic characteristics of europium and ytterbium compounds, which distinguish them from those of the compounds of other lanthanides, are probably determined by the nature of the interaction of various elements with the 5*d* electrons of the lanthanides.

If the formation of the compound requires three valence electrons of the lanthanide, then in the case of europium and ytterbium, which have only two valence electrons in the metallic state under standard conditions[6], $4f-5d$ transitions, accompanied by an increase in the number of valence electrons to three and a corresponding energy expenditure (22 ± 2 kcal mole^{-1} for europium and 9 ± 2 kcal mole^{-1} for ytterbium), take place. The Gibbs free energies and enthalpies of formation of the europium and ytterbium compounds are then smaller than the corresponding quantities for the formation of similar compounds of the adjacent lanthanides.

When the enthalpies of formation of europium or ytterbium compounds fit the general variation of the enthalpies of formation of lanthanide compounds, it is postulated[315] that the third valence electron of the lanthanide (a 5*d* electron[6,347]) is not involved in the formation of the chemical bond (or its contribution to the bond energy is small), is delocalised, and is responsible for the metallic conduction. Europium and ytterbium compounds of this type (for example monochalcogenides[179]), in which there are only two valence electrons (i.e. in europium and ytterbium)[179], may prove to be semiconductors or insulators.

We shall consider the thermochemical behaviour of europium and ytterbium, involving a greater ease (on energy grounds) of the interaction of a non-lanthanide element with europium or ytterbium than with adjacent lanthanides, from the standpoint of the configurational model of matter developed by Samsonov and coworkers[348-350] using as an example lanthanide–calcium alloys. The valence electrons of calcium in the excited state do not include more than one *d* electron per atom and tend to assume the d^0 configuration. The valence electrons of the lanthanides (except for europium and ytterbium) include one–two *d* electrons per atom and also tend to assume the d^0 configuration. In the calcium–lanthanide system each component tends to give up its valence *d* electron to the other component. This leads to an antagonism between calcium and the lanthanide, the separation of the liquid alloys into two phases[6], and positive Gibbs free energies, enthalpies, and entropies of mixing of the components[346]. Europium and ytterbium do not have 5*d* electrons and their mixing with calcium involves a decrease in enthalpy[346].

In compounds of the type LnN and $LnIr_2$ lanthanum is tervalent and cerium is quadrivalent[6] (the "true" valence is determined by the number of electrons delocalised from the given atom[351]). The Gibbs free energies and enthalpies of formation of CeN and $CeIr_2$ are higher than those for LaN and $LaIr_2$ respectively. This combination of the thermodynamic characteristics of the lanthanum and cerium compounds shows that the contribution of the fourth valence electron of cerium to the energy of the chemical bond with nitrogen and iridium is fairly large, particularly since the increase of the number of valence electrons of cerium from three in the pure metal to four in the compound requires an energy of about 50 kcal g-atom^{-1}.[36] It has been established that the change in the number of valence electrons from three in metallic samarium to two in the compound involves a change in the Gibbs free energy and enthalpy of 6.2 ± 1.7 kcal g-atom^{-1} under standard external conditions[352].

The variation of the Gibbs free energies and enthalpies of formation of binary lanthanide compounds as a function of the atomic number of the element is complex. On passing from lanthanide trichlorides to oxides, the stability series is inverted. Whereas in the trichloride series the maximum enthalpy of formation corresponds to $LaCl_3$ (Table 1), in the series La_2O_3–Gd_2O_3–Lu_2O_3 the maximum corresponds to Lu_2O_3 (Table 2). The enthalpies of formation of lanthanide dicarbides (Table 8) and dihydrides (Table 10) remain virtually constant from lanthanum to lutetium. The variation of the enthalpies of formation of the solid lanthanide compounds has been considered on the basis of the concepts of the energy of stabilisation by the crystal field[1,3,34,353,354], the promotion energy, and bond multiplicity[355,356]. The observed relations are largely qualitative.

The dissociation energies of gaseous lanthanide compounds decrease in the series from lanthanum to europium and from gadolinium to ytterbium. Charkin[357] showed that the variation of the dissociation energies in the series of lanthanide compounds is determined by the variation of the excitation energies of the valence electron configurations of the lanthanides. It has also been shown[16,165] that the dissociation energies of the compounds vary with the degree of involvement of the lanthanide *d* electrons in the formation of chemical bonds. However, the nature of the relation between the dissociation energies of lanthanide monoxides or monosulphides and the same series of degrees of involvement of *d* electrons, calculated[358] from the properties of the lanthanides alone, remains obscure. Apparently the degrees of involvement of $4f$, $5d$, $6s$, and $6p$ valence electrons of the lanthanide in the formation of chemical bonds and hence the set of valence electron configurations can nevertheless change on passing from one class of lanthanide compounds to another (particularly in the solid state). This in fact leads to different changes in the thermodynamic characteristics in the series of solid lanthanide compounds. The proposed explanation of the variation of the Gibbs free energies or enthalpies of formation in the series of lanthanide compounds is consistent with Gschneidner's study[359], where four types of relations between the degree of involvement of $4f$ electrons in the chemical bond and the atomic number of the element were established on the basis of 33 series of lanthanide compounds.

In conclusion we may note that the thermodynamic characteristics of lanthanide compounds have been used[191,360] to determine the type of chemical bond. Comparison of the experimental and calculated enthalpies of formation of intermetallic lanthanide compounds showed[360]

that there is a predominantly metallic type of bond in the intermediate compounds of the lanthanide–magnesium systems; in lanthanide alloys with *p* elements there is a considerable contribution by ionic-covalent bonding. Thus the study of the thermodynamics of the interaction of the lanthanides with various elements permits certain conclusions concerning the nature of the valence electrons involved in the formation of the chemical bond and the type of bond in the compounds formed.

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The Structure and Methods of Synthesis of Thiirans

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The data presented in the review confirm the earlier results concerning a structural similarity between the two-carbon skeleton of the thiiran ring and the double bond of alkenes.
The available data on the syntheses and structures of thiirans and alkene episulphoxides and episulphones are treated systematically. The methods for the formation of the thiiran ring are classified and synthetic procedures based on homolytic, anionotropic, and cationotropic closure of thiiran rings and on thiiran reactions occurring without the opening of the ring are discussed.
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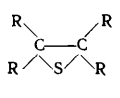
I. INTRODUCTION

Thiirans (alkylene sulphides or epithioalkanes) are saturated sulphur-containing three-membered heterocyclic compounds with structure (I). The thiiran 1-oxides (II) and 1,1-dioxides (III) can also be included in this group.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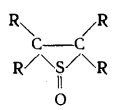
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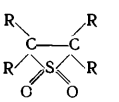

(III)

Until recently thiirans were believed to be of purely theoretical interest, their chemistry being investigated to elucidate the nature of three-membered heterocyclic compounds, but in the last few years the attitude towards these substances changed radically. The accumulated information about the properties and reactivities of thiirans made a significant contribution to theoretical organic chemistry and demonstrated the wide scope of their applications in syntheses of polymeric substances, physiologically active compounds, detergents, oil additives, etc.

More than 400 studies have now been made on the properties and methods of synthesis of thiirans. Almost half of these have been discussed in previous reviews[1-9]. The considerable advances achieved in the chemistry of thiirans during the last decade led us to undertake a new survey of the available information about this interesting branch of organic chemistry.

In contrast to previous reviews on thiirans, in the present article attention has been concentrated on a systematic arrangement of the data. The available information about the structures of thiirans is discussed critically, the known methods of thiiran synthesis are classified, and the mechanisms of the closure of thiiran rings are considered. In order to elucidate in greater detail certain problems, analogies have been drawn between thiirans and their heteroanalogues—oxirans and aziridines.

The limited size of the review precluded a detailed description of all the problems involved in the topic under consideration. The present state of thiiran chemistry is described on the basis of publications during the last two decades. Earlier communications are quoted only when necessary to illustrate certain postulates.

II. THE STRUCTURE OF THIIRANS

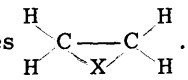
The problems concerning the structure of three-membered cyclic compounds have been the subject of a lively discussion begun by Walsh[10] in 1947, who considered Zimakov's concepts[11] in relation to the characteristics of the structure of oxiran. In the course of the discussion and subsequent studies, significant arguments were adduced, demonstrating the structural similarity between cyclopropane[12] and particularly its heteroanalogues on the one hand and ethylenic hydrocarbons on the other.

One of the first pieces of evidence confirming certain structural analogies between cyclopropane, oxiran, thiiran, and alkenes was obtained by Linnett[13]. The force constants of the C–H bonds in methylene groups, which he calculated from Raman and infrared spectra, proved to be 5 for cyclic compounds and 5.1 for ethylene. The closeness of these values and their considerable difference from the constants of the C–H bonds in the methylene groups of paraffins (4.6) indicate, according to the author, a greater similarity between the valence states of the carbon atoms in cyclopropane and its heteroanalogues to those in ethylenic compounds compared with the corresponding states in paraffins. This conclusion was confirmed by subsequent studies on the structures of cyclopropane heteroanalogues.

The results of electron diffraction studies on aziridine[14,15], oxiran, and thiiran[16] (Table 1) suggest that the transformation of an acyclic compound into a three-membered heterocycle is accompanied by a rearrangement of the hybrid states of the atoms forming the ring. The C–C bond lengths in all these compounds are similar and intermediate between the C–C bond length in diamond (1.544 Å) and the C=C bond length in ethylene (1.344 Å). It is interesting to note that the distance between the carbon atoms in cyclopropane heteroanalogues is close to the length of the central bond in butadiene (1.483 Å), which can be regarded, according to Dewar's ideas[17], as a simple sp^2–sp^2 σ bond. The C–H bond lengths in cyclopropane heteroanalogues are similar to the corresponding bond lengths in ethylene (1.086 Å), while the HCH angle exceeds by 6.5–6.9° the tetrahedral angle and approaches the HCH angle in ethylene. The lengths of the bonds

between the carbon atoms of the ring and the heteroatom are equal or slightly greater than the lengths of the corresponding bonds in acyclic amines, ethers, and sulphides.

The above data on the structures of cyclopropane heteroanalogues suggest that their molecules contain two types of *endo*-bonds. The two-carbon skeleton has an enhanced *s* character compared with the saturated C–C bond. According to its fundamental parameters, this bond approaches the σ bond in ethylene. The remaining two *endo*-bonds are formed from the *p* electrons of the heteroatom and the partly hybridised *p* electrons of the carbon atoms. This results in a type of overlapping of atomic orbitals which is intermediate between the lateral π-bonding and terminal σ-bonding overlapping.

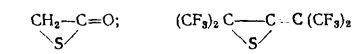
The principal parameters of the molecules  .

Parameter	X		
	NH	O	S
Bond length, Å			
C—C	1.480	1.467	1.492
C—H	1.083	1.082	1.078
C—X	1.488	1.436	1.819
HCH angle	116°41′	116°41′	116°00′
CXC angle	—	61°24′	65°48′

The electronic state of the heteroatoms in aziridine, oxiran, and thiiran can be inferred only from certain indirect data. The studies of the ability of three-, four-, and five-membered heterocycles to form a hydrogen bond with phenol[18], of their capacity for complex formation with iodine[19], and of their heats of solution in chloroform[20] indicate an enhanced *s* character of the free electrons of the heteroatom in three-membered heterocycles compared with four- and five-membered heterocyclic compounds and acyclic amines, ethers, and sulphides. This is also indicated by the chemical shifts of the α- and β-CH_2 groups in the NMR spectra of cyclopropane heteroanalogues[21,22]. Thus the formation of a three-membered heterocycle entails a change in the electronic states not only of carbon atoms but also of the heteroatom in the ring.

The enhanced *s* character of the lone electron pairs of the heteroatoms is evidence for the presence of an unusual conjugated system in molecules of cyclopropane heteroanalogues. It is quite likely that the sharp differences between the ring strain energies of cyclopropane on the one hand (25 kcal $mole^{-1}$ [23]) and aziridine, oxiran, and thiiran (14, 13, and 9 kcal $mole^{-1}$ respectively) on the other are due to the stabilisation of the cyclic state in heterocyclic compounds by the π-electrons of the heteroatoms.

The above features of the structures of cyclopropane heteroanalogues are shown most clearly in the series of thiiran compounds owing to the greater covalent radius of the sulphur atom compared with those of the nitrogen and oxygen atoms and the high lability of its 3*p* electrons. The enhanced sp^2–sp^2 character of the C–C bond in thiirans has been confirmed, apart from the data quoted above, by a study of the structure of propylene sulphide [2-methylthiiran][24]. The CH_3–CH bond length (1.513 Å) is smaller than the C–C bond length in diamond by an amount equal to the difference between the effective covalent radii of the carbon atom in the sp^3- and sp^2-hybrid states, which suggests that the bond is of the sp^3–sp^2 type. The existence of 2-thiiranone[25] and 3-hexafluoroisopropylidene-2,2-bistrifluoromethylthiiran[26],



may be regarded as one of the pieces of evidence confirming the sp^2 hybrid state of the carbon atoms in the thiiran ring.

The enhanced *s* character of the C–C bond in thiirans is due to the pronounced *p* character of the C–S bond. In the ethylene sulphide [thiiran]–ethylene sulphoxide–ethylene sulphone series the inclusion of the sulphur *p* electrons in additional valence bonds lowers the stability of the thiiran ring and alters the nature of the C–C bonds. The C–C bond length calculated from microwave spectra of ethylene sulphone[27] proved to be 1.586 ± 0.01 Å. This suggests that the carbon atoms of the thiiran ring in ethylene sulphone are in the sp^3 hybrid state.

The pronounced *p* character of the C–S bond is responsible for the pseudo-unsaturated character and the electrophilic properties of thiirans, which has been confirmed by spectroscopic studies on phenylthiirans substituted in the *para*-position[28]. It is quite likely that vacant 3*d* orbitals of the sulphur atom contribute to the π-electron density of the thiiran ring, because a satisfactory agreement has been achieved between experimental and calculated spectroscopic characteristics when account was taken of not only 3*s* and 3*p* but also 3*d* levels of this element[29].

The enhanced pseudo-unsaturated character of the thiiran ring is responsible for its greater stability compared with the oxiran ring, which has been confirmed by a comparative study of the behaviour of *p*-methoxyphenyloxiran and *p*-methoxyphenylthiiran under solvolysis conditions[30]. The greater stability of the thiiran ring compared with the oxiran ring is also indicated by lower strain energy of the thiiran ring (relative to the oxiran ring), determined from the difference between the heat of formation and the sum of the individual bond energies[32], and by the lower strain entropy and enthalpy of thiiran compared with oxiran[30] (59.19 e.u. and 38.44 kcal $mole^{-1}$ for oxiran and 21.47 e.u. and 17.62 kcal $mole^{-1}$ for thiiran).

The thiiran molecule can be represented, like those of aziridine and oxiran, by an asymmetric rotator with the symmetry plane perpendicular to the plane of the C–C ring. For this reasons, its 2,3-disubstituted derivatives exist as two geometrical isomers (*cis*- and *trans*-). The internally compensated *cis*-isomers of the symmetrical 2,3-disubstituted thiirans are optically inactive. Monosubstituted thiirans, the *trans*-isomers, and the *cis*-isomers of 2,3-disubstituted thiirans can be obtained in an optically pure state[31–35].

III. METHODS FOR THE SYNTHESIS OF THIIRAN COMPOUNDS

The reactions of acyclic or certain cyclic compounds leading to the formation of three-membered sulphur-containing rings are most frequently used to synthesise thiirans. However, methods based on reactions of thiirane derivatives without ring opening have also been used successfully in many instances.

1. METHODS BASED ON THE HOMOLYTIC CLOSURE OF THIIRAN RINGS

a. Addition of Sulphur to Alkenes

The early attempts to add atomic sulphur formed in the pyrolysis of diethyl tetrasulphide to ethylene, propene, and cyclohexene were relatively ineffective [36]. The yield of thiiran derivatives did not exceed several per cent in view of the low yield of atomic sulphur in the reaction

$$R{-}CH{=}CH_2 + C_2H_5(S)_4C_2H_5 \xrightarrow{150^\circ} R{-}\underset{\diagdown S \diagup}{CH{-}CH_2} .$$

Best results were obtained using carbon oxide sulphide as a source of atomic sulphur [37-39]. Irradiation of a mixture of carbon oxide sulphide in ethylene or propene with ultraviolet light (255–229 nm) at 25°C leads to the formation of the corresponding thiirans in a yield of 60–100% relative to the olefin which has reacted. However, the degree of conversion of alkenes in such reactions is very low. 1,2-Epithiobutene [2-ethylthiiran], *cis*- and *trans*-butylene sulphides, and isobutylene sulphide [2,2-dimethylthiiran] were obtained in low yields under the same conditions. Only butadiene reacts anomalously under the conditions of photolytic sulphur addition, giving rise to vinyldithiacyclobutane and thiophen [40].

Under photolysis conditions, hexafluorocyclobutene is readily acted upon by atomic sulphur [41]. The resulting perfluorocyclobutylene sulphide is unstable and has a half-life of about 1 min at 20°C. Tetrafluoroethylene reacts at 445° with elemental sulphur to form a mixture of tetra-, tri-, and mono-sulphides [42,43]. Tetrafluorothiiran was obtained under these conditions in a yield of 2%.

The formation of thiirans on reaction with sulphur under photolysis conditions is a typical free-radical process. The sulphur atom in both the singlet and triplet states enters readily into this reaction [38], which proceeds with a low activation energy [39]. Under the reaction conditions, the formation of the thiiran is accompanied by its photolytic decomposition, which is the reason for the low degree of conversion of alkenes in this reaction.

$$R{-}CH{=}CH_2 + S^* \rightarrow R{-}\underset{\diagdown S \diagup}{CH{-}CH_2} \xrightarrow{S} R{-}CH{=}CH_2 + S_2 .$$

A careful study [43] has shown that the high-temperature reaction of tetrafluoroethylene with sulphur proceeds via a stage involving the formation of difluorocarbene:

$$CF_2{=}CF_2 \xrightarrow{>400^\circ} :CF_2 \xrightarrow{S} CF_2{=}S \xrightarrow{CF_2:} \underset{\diagdown S \diagup}{CF_2{-}CF_2} .$$

b. Condensation of Sulphur and Its Compounds with Diazoalkanes

This reaction was historically the first process whereby it was possible to obtain thiirans as individual compounds. Before its discovery, the formation of thiirans in reactions was inferred only from the evolved polyalkylene sulphide [44,45] and it was believed that these substances do not exist in a monomeric state [45].

In 1916–1920 Staudinger and coworkers [46-48] reported the formation of thiirans in the reaction between diazoalkanes and aromatic thioketones, thiophosgene, and thiobenzoyl chloride:

$$RR'CN_2 + R''R'''C{=}S \rightarrow \underset{\diagdown S \diagup}{RR'C{-}CR''R'''} .$$

The reactions proceed smoothly at room temperature and the final products are isolated in high yields after the evolution of nitrogen ceases.

The scope of Staudinger's method for the synthesis of thiirans and also some of the limitations in their applications have been determined in studies by Schonberg and coworkers [49-56]. According to their data, thiobenzophenones, thioxanthene, and other aromatic cyclic thioketones react unambiguously only with diaryldiazomethanes. The reactions with diazomethane, diazoethane, and ethoxycarbonyldiazomethane result in the formation of 1,3-dithiolans:

$$Ar_2C{=}S + R{-}CHN_2 \rightarrow \begin{array}{c} Ar_2C{-}CAr_2 \\ | \quad\quad | \\ S \quad\quad S \\ \diagdown CH \diagup \\ | \\ R \end{array} .$$

Thiirans have also been obtained by the reaction of diaryldiazoalkanes with other thiono-compounds, including diphenyl trithiocarbonate, the chlorides of phenyldithiocarbonic and phenylthiocarbonic acids, and xanthogen sulphide:

$$Ar_2CN_2 + S{=}\overset{X}{\underset{Y}{C}} \rightarrow Ar_2C\overset{X}{\underset{S \quad Y}{\diagup \quad \diagdown}}C .$$

(X=SC_6H_5; Cl; SC(S)OR; OC_6H_5; Y=SC_6H_5; OC_6H_5; OR)

The reaction of diazoethane with thiocarbonic acid derivatives is similar to that of diaryldiazomethanes [52]. However, in this case too diazomethane reacts anomalously with formation of 1,3-dithiolan derivatives.

Aliphatic thioketones have recently been successfully introduced into the reaction with diazoalkanes [57]. In this case the reaction involving diazomethane yielded the normal condensation products—2,2-disubstituted thiirans:

$$RR'C{=}S + CH_2N_2 \rightarrow \underset{\diagdown S \diagup}{RRC{-}CH_2} .$$

Cycloalkenethiones react with diazoalkanes to form a complex mixture of products from which thiirans, dithiolans, and alkenes were isolated [58]. The reactions of diazomethane [59], diazoethane, and dimethyldiazomethane [60] with thioketones and thio- and dithio-carboxylates led to the isolation, together with thiirans, of olefins and 1,2,3- and 1,3,4-thiadiazolins. In certain cases, for example in the reaction between fluorenethione and diphenyldiazomethane [64], the only products were alkenes.

In contrast to aromatic thioketones [65], hexafluorothioacetone readily forms 2,2-bis(trifluoromethyl)thiirans not only on reaction with diphenyldiazomethane but also with ethoxycarbonyldiazomethane [61]. The fluoride of perfluorothiopropionic acid also reacts with diazoalkanes, but the resulting thiirans readily undergo spontaneous sulphur elimination and the final outcome of such reactions is the formation of alkenes [62]:

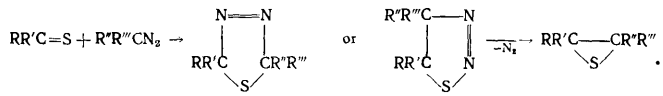
$$CF_3CF_2C(S)F + (C_6H_5)_2CN_2 \rightarrow \underset{\diagdown S \diagup}{CF_3CF_2CF{-}C(C_6H_5)_2} \xrightarrow{-S} CF_3CF_2CF{=}C(C_6H_5)_2 .$$

Thiocarbonyl fluoride enters into exchange reactions with diphenyldiazomethane [43,63], which leads to the formation of tetraphenylthiiran:

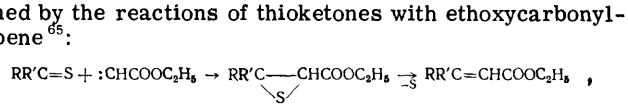
$$2(C_6H_5)_2CN_2 + CF_2{=}S \rightarrow \underset{\diagdown S \diagup}{(C_6H_5)_2C{-}C(C_6H_5)_2} .$$

The mechanism of the complex reactions in thiono-compound–diazoalkane systems has not been investigated thoroughly. The hypothesis that the diazoalkane initially

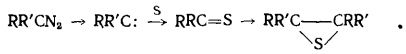
undergoes the Pechmann condensation with the thiono-compound to form 1,2,3- or 1,3,4-thiadiazolin, whose decomposition with liberation of nitrogen is accompanied by a free-radical closure of the thiiran ring at the C–C or C–S bond, is quite likely:



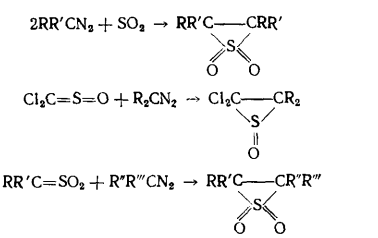
All the reactions in such systems can also be accounted for on the hypothesis of the initial formation of carbenes in the reaction mixture. The addition of the latter to the C=S bond can lead to the formation of both a thiiran and a 1,3-dithiolan. The latter mechanism of the formation of thiirans from thiono-compounds and diazoalkanes is confirmed by the reactions of thioketones with ethoxycarbonylcarbene [65]:



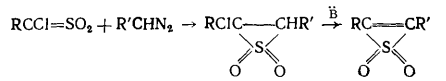
and also by the reactions of diazoalkanes with sulphur [64,66], which take place readily under the usual conditions of the above syntheses, where the formation of a carbene is the most likely process:



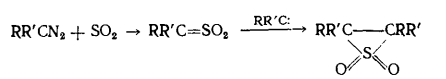
The ability to condense with coordination-unsaturated sulphur compounds is a common property of diazoalkanes. Apart from thiono-compounds and sulphur, sulphur dioxide [67–76] and sulphenes [77–80] react smoothly with diazoalkanes:



These reactions do not always proceed unambiguously. In certain cases alkenes [71] or derivatives of 1,3,4-thiodiazines are the side products of these processes [70,79]. 3-Alkyl-2-halogenothiiran 1,1-dioxides are converted under the reaction conditions into thiiren 1,1-dioxides:

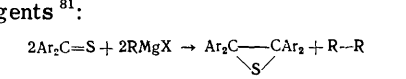


The mechanism involving the preliminary formation of carbenes is regarded as the most likely pathway to the formation of the thiiran 1,1-dioxide ring [76]:

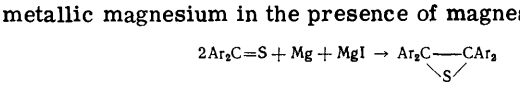


c. Condensation of Thiones with Carbenes

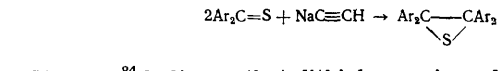
In 1927 Schonberg et al. reported the formation of tetra-arylthiirans in reactions of thiobenzophenones with Grignard reagents [81]:



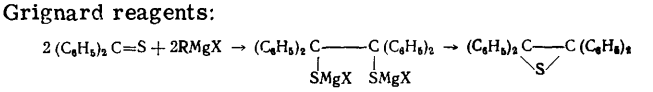
The results of this reaction is independent of the nature of the organomagnesium compound: thioketones react readily with alkyl- or aryl-magnesium bromides or iodides and are converted into thiirans in high yields. Similar results were obtained on treating thioketones with metallic magnesium in the presence of magnesium iodide [82]:



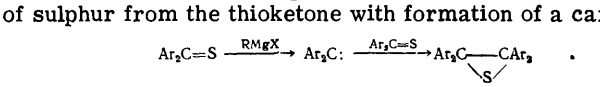
Later the formation of thiirans was observed on treating thioketones with sodium acetylide [83]:



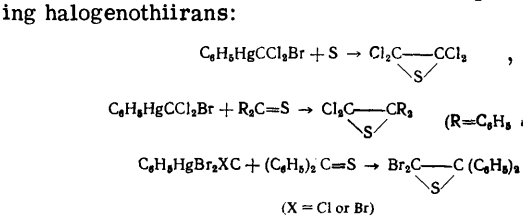
Moreau [84] believes that dithiobenzopinacol is an intermediate in the reaction between thiobenzophenone and Grignard reagents:



However, a recent investigation of these reactions [85] led to the conclusion that the primary step is the elimination of sulphur from the thioketone with formation of a carbene:

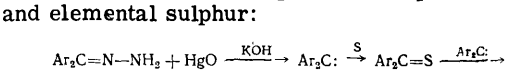


The condensation of carbenes with sulphur and thiones have been widely investigated by Seyferth et al. [86], who used various phenyl(trihalogenomethyl)mercury compounds as a source of carbenes. The bromodichloro-, dibromochloro-, and tribromo-methyl derivatives react smoothly with sulphur, thiophosgene, and thiobenzophenone, forming halogenothiirans:



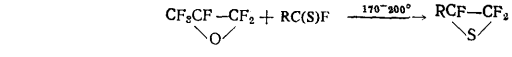
Only phenyl(trifluoromethyl)mercury fails to form a thiiran in the reaction with thiobenzophenone [87].

The marked ability of carbenes to react with elemental sulphur and thiones has been used to develop a simple preparative method for the synthesis of tetra-arylthiirans [88,89]. It consists in treating ketone hydrazones with mercury(II) oxide in the presence of potassium hydroxide and elemental sulphur:



The conversion of phenylmethanesulphonyl chloride into 2,3-diphenylthiiran on heating with triethylamine in methylene chloride or ether probably also involves the formation of a carbene [90].

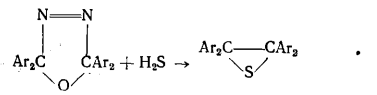
The possibility of synthesising polyfluorothiirans by pyrolytic reactions of fluoro-compounds with formation of difluorocarbene in the presence of sulphur and its compounds has been demonstrated in a number of studies. These syntheses include the high-temperature combination of tetrafluoroethylene with sulphur [43] and the reactions of 2,2,3-trifluoro-2-trifluoromethyloxiran with thiocarbonyl fluoride, thiocarbonyl chloride fluoride, and perfluorothioacyl fluorides also belong to syntheses of this type [49,91–94]:



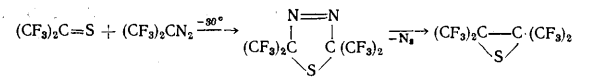
The yield of polyfluorothiirans under these conditions is usually low owing to the occurrence of side reactions involving the final products, in which they undergo sulphur elimination and isomerisation.

d. Syntheses of Thiirans by the Pyrolysis of Heterocyclic Compounds

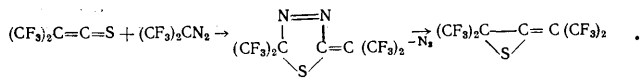
There are at present few examples of these reactions. In 1939 Schonberg and Barakat [95] showed that thiirans are formed in high yields on heating oxadiazines in an atmosphere of hydrogen sulphide:



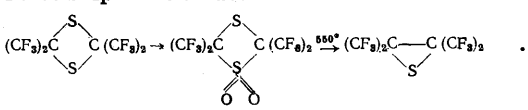
Middleton [26] obtained from perfluorothioacetone and bis(trifluoromethyl)diazomethane under mild conditions 2,2,5,5-tetra(trifluoromethyl)-1,3,4-thiadiazine, which he converted into tetra(trifluoromethyl)thiiran by pyrolysis:



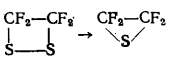
Bis(trifluoromethyl)thioketen reacts similarly to hexafluorothioacetone. The first example of thiirans whose ring is linked to the substituent by a C=C bond was obtained in this way:



Middleton also developed a method for the preparation of perfluoro-derivatives of tetra-alkylthiirans from thioketone dimers [96]. By oxidising the latter with chromium trioxide in nitric acid, he obtained sulphones which he converted into thiirans by pyrolysis over platinum in an atmosphere of sulphur dioxide:



Tetrafluorothi-iran was obtained together with other products also in the pyrolysis of tetrafluorodithiacyclobutane [94]:

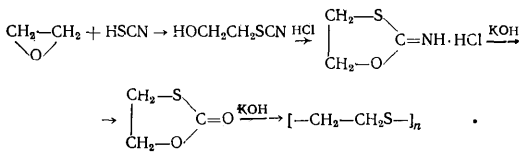


There is no doubt that the above syntheses of thiirans have a free-radical mechanism. In many of these, except the last, a homolytic closure of the thiiran ring with formation of a C–C bond takes place.

2. REACTIONS INVOLVING THE ANIONOTROPIC SUBSTITUTION OF THE OXYGEN ATOM IN OXIRANS BY A SULPHUR ATOM

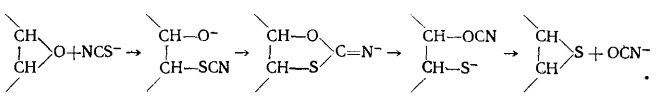
The syntheses of thiirans by the reaction of their oxygen analogues with alkali metal thiocyanates and thiourea have now become classical and are recommended for use on a preparative scale as the most convenient procedures of this kind [97].

The history of the devlopment of this method has been described in very great detail in Weissberger's review [7] and one need only note that all the stages of the conversion of oxiran into thiiran in the reaction of the former with thiocyanates were first described in 1937 by Sergeev and Kolychev [98]. Having obtained 2-thiocyanatoethanol by the reaction of oxiran with thiocyanic acid, the authors converted it almost quantitatively into the hydrochloride of ethylene monothiocarbonate imine [the hydrochloride of 2-imino-1,3-oxathiolan]. The latter was converted on treatment with an equivalent amount of alkali into ethylene monothiocarbonate [2-oxo-1,3-oxathiolan] and with an excess of alkali into poly(ethylene sulphide).



On the basis of the results of Sergeev and Kolychev [98], Ettlinger [99] proposed a mechanism for the reaction of oxirans with alkali metal thiocyanates whose validity was proved rigorously by van Tamelen [100] and independently by Price and Kirk [31].

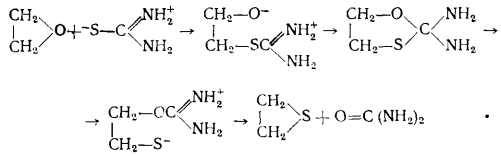
Ettlinger believes that the formation of thiirans in these reactions involves the nucleophilic opening of the oxiran ring by the thiocyanate anion, the isomerisation of the resulting alkoxide anion via an intermediate cyclic state into a thiolate anion, and the conversion of the latter into the thiiran with elimination of the cyanate anion:



According to this mechanism, the conversion of the oxiran ring into a thiiran ring should involve two Walden inversions in the *trans*-opening and *trans*-closure of the ring. Only oxirans derived from acyclic and unstrained cycloalkenes can be expected to give rise to thiirans. Those derived from strained cycloalkenes should not react, because the formation of an intermediate bicyclic ion with two strained rings by *trans*-closure is impossible.

Van Tamelen showed that cyclohexenylene oxide {cyclohexeno[*b*]oxiran} reacts with potassium thiocyanate, 2-thiocyanatocyclohexanol, and the hydrochloride of cyclohexenylene monothiocarbonate imine {the hydrochloride of 2-iminocyclohexeno[*d*]1,3-oxathiolan} and is smoothly converted into cyclohexenylene sulphide {cyclohexeno[*b*]thiiran} in the presence of bases. Cyclopentenylene sulphide {cyclopenteno[*b*]thiiran} is not formed from the corresponding oxiran and potassium thiocyanate. Price and Kirk showed that an intermediate iminoether is formed in the reaction between 2-methyloxiran and potassium thiocyanate, having isolated it in the form of the 4-nitrobenzoate. Moreover they obtained L(–)-2,3-dimethylthiiran by the reaction of D(+)-2,3-dimethyloxiran with potassium thiocyanate. All these findings are consistent with Ettlinger's ideas concerning the mechanism of the conversion of oxirans into thiirans.

A similar mechanism for the formation of thiirans in the reaction of oxirans with thiourea was proposed by Culvenor et al.[101]:



Bordwel and Andersen[102] believe that the transition state in this process is formed from a neutral molecule of *S*-(2-hydroxyalkyl)isothiourea and not from the 2-alkoxyisothiuronium ion. They base this view on the observation that high yields of thiirans are obtained only in media with a pH close to 7.

The mechanisms proposed by Ettlinger and Culvenor for the conversion of oxirans into thiirans were confirmed further by recent studies on the reactions of potassium thiocyanate and thiourea with optically active 2-phenyloxiran, 2-methyl-3-phenyloxiran, and 2,3-diphenyloxiran[35]. It was shown that the conversion of the above compounds into thiirans entails the inversion of the configuration of the initial molecule at both carbon atoms of the ring, which can only be understood when account is taken of the formation of cyclic transition states in the reaction.

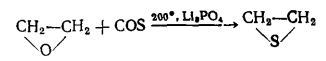
The scope of the synthesis of thiirans from oxirans by reaction of the latter with alkali metal thiocyanates or thiourea is very great. Thiiran and 2-methylthiiran[103-105], the *cis*- and *trans*-isomers of 2,3-dimethylthiiran[31,34], 2,3-dimethylthiiran[103], 2-hexylthiiran[106], 2-diethoxymethylthiiran[107], 2-vinylthiiran[108], cyclohexeno[*b*]thiiran and its derivatives[103,108], 2-chloromethylthiiran[103], alkoxy- and aryloxy-methylthiirans[109-113], alkylthiomethyl- and dialkylaminomethyl-thiirans[100,113], 2-phenylthiiran and its ring-substituted derivatives[28,35,114,115], esters of epithiodienecarboxylic acids [thiiranylalkenecarboxylic acids][116], 4-piperidinylthiirans[33], and other compounds have been obtained by this method.

The extensive studies on these reactions by Culvenor et al.[108] showed that only thiirans with electronegative groups attached to the thiiran ring cannot be obtained by this method because of the ease of elimination of sulphur in the course of their formation. However, later investigations established that under certain conditions of synthesis even thiirans which readily lose sulphur can be obtained from oxirans. For example, *cis*- and *trans*-2,3-diphenylthiirans were obtained in yields up to 90%[117] under the conditions of the Bordwel synthesis by the initial condensation of the corresponding oxirans with thiourea sulphate and subsequent cautious alkaline treatment of the resulting isothiuronium salts.

The yields of thiirans in the reactions of oxirans with alkali metal thiocyanate of thiourea are 30–80% and depend significantly on the process conditions. The reactions are usually carried out at 0–20°C under homogeneous conditions, using water, lower alcohols[101-103,108], and mixtures of alcohol and acetic acid[118] as solvents. According to patent data[119], a higher yield of thiirans is achieved when anhydrous polar solvents are used.

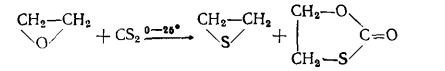
Ammonium thiocyanate, aryl- and diaryl-thioureas, thiocarboxylic acid amides, and certain thiocarboxylic acids have been used instead of alkali metal thiocyanates and thiourea[24,103]. The reactions with these substances take place under the conditions of the synthesis of thiirans from oxirans by reaction with thiourea or alkali metal thiocyanates.

Industrial methods for the synthesis of thiirans from their oxygen analogues and readily available sulphur-containing compounds, such as carbon oxide sulphide and carbon disulphide, are now being developed. Durden et al.[120] showed that at 150°C oxiran forms a copolymer with carbon oxide sulphide in the presence of bases. However, when these substances are brought into contact over a basic catalyst under more severe conditions (at about 200°C), thiiran is formed. The best catalyst for these reactions proved to be trilithium phosphate:



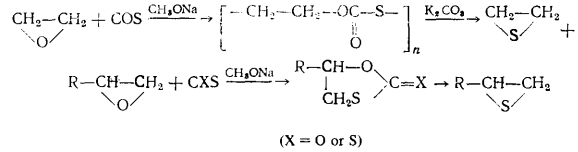
According to patent data, the formation of thiirans from oxirans and carbon oxide sulphide or carbon disulphide in the vapour phase is catalysed by sodium fluoride, its mixtures with other sodium halides, the halides of other alkali and alkaline earth metals, alkaline earth metal oxides, and alkali metal sulphides[121-123]. The yield of low-boiling thiirans reaches 90% in relation to the oxiran which has reacted.

Thiiran can be obtained in yields up to 80% from oxiran and carbon disulphide in the presence of a mixed catalyst consisting of partly hydrated lithium chloride and triethylsulphonium iodide[124,125]. Ethylene monothiocarbonate-[2-oxo-1,3-oxathiolan] is a side product:



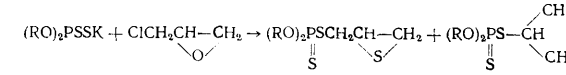
Somewhat less satisfactory results were obtained when the reaction was catalysed by lithium chloride in the presence of hydrogen sulphide[126]. The main products in the presence of these catalysts are ethylene mono- and dithiocarbonates [2-oxo-1,3-oxathiolan and 2-oxo-1,3-dithiolan] and thiiran is formed in yields up to 20%.

When the catalyst is sodium methoxide, the above reactions give rise to polymeric substances[127] or alkylene mono- and di-thiocarbonates [alkyl derivatives of 2-oxo-1,3-oxathiolan or 2-oxo-1,3-dithiolan][128,129], which can be converted into thiirans on heating with alkaline agents:



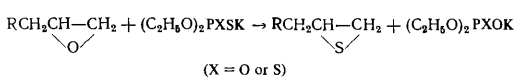
(X = O or S)

Interesting reactions involving the conversion of 2-chloromethyloxiran into derivatives of 2-methylthiiran have been described by Schroder[130]. According to his data, the reactions of 2-chloromethyloxiran with an excess of salts of *OO*-dialkylphosphorodithioic acid in water lead to *OO*-dialkyl *S*-thi-iranylmethyl phosphorodithioates. These data were confirmed by Nuretdinova[131], who also showed that small amounts of thietan derivatives are formed in the reactions together with thiirans:



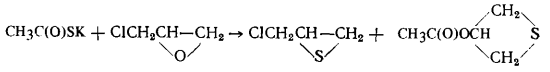
Arbuzov and Nuretdinova[132,133] studied the reactions of 2-chloromethyloxiran, 2-methyloxiran, glycidyl phenyl ether [2-phenoxymethyloxiran], and *OO*-diethylphosphonomethyloxiran with thiolic acid salts. Potassium salts of

phosphorothioic and phosphorodithioic acids react smoothly with oxirans and the corresponding thiirans were isolated in yields of 40–55%:

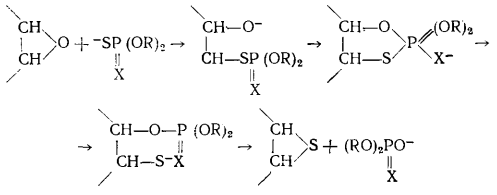


(X = O or S)

On reaction with the triethylammonium salt of *OO*-diethylphosphorodithioic acid, 2-chloromethyloxiran is also converted into 2-chloromethylthiiran. However, the reaction with thioacetic acid salts gives rise to a mixture of 2-chloromethylthiiran and 3-acetoxythietan:



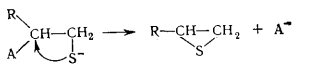
The mechanism of the conversion of oxirans into thiirans by the reactions with thiolic acid salts is satisfactorily consistent with the scheme devised by Ettlinger and Culvenor:



The validity of this scheme is also confirmed by the susceptibility of *S*-(2-hydroxyethyl) esters of thiocarboxylic and phosphorothioic acids [134] to cleavage by bases with formation of thiirans or their polymers. The formation of thiirans in the acid-catalysed reaction of oxirans with phosphine sulphides [135] also proceeds in accordance with Culvenor's mechanism

The marked influence of the polarity of the solvent must be regarded as a characteristic feature of the above methods of synthesis of thiirans from oxirans. In an aqueous homogeneous medium the process is usually exothermic. Heat is required for the reaction in less polar solvents. This is due primarily to the specific features of the anionotropic reactions in ionic alkoxide–thiolate rearrangements and in the closure of the thiiran ring. The driving force in the first process is provided by the high energy of the thioacyl linkage. The favourable effect of the polar solvent is in this case evident, as in other instances of the nucleophilic substitution at coordination-unsaturated carbon and phosphorus atoms.

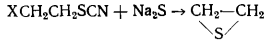
The completion of the stage involving the formation of thiiran rings from oxiran rings is very similar in all the cases considered. The conversion of the thiolate anion into thiiran can be regarded as anionotropic ring closure with elimination of the weaker nucleophile (the alkoxide anion):



The anionotropic closure of the thiiran ring is promoted by the comparatively low enthalpy associated with the thiiran ring strain, the low capacity for solvation and hence the high reactivity of the thiolate anion, and the marked influence of the solvolysis of the eliminated alkoxide anions.

3. THE ANIONOTROPIC FORMATION OF THIIRANS FROM 2-SUBSTITUTED ALKANETHIOLS AND THEIR DERIVATIVES

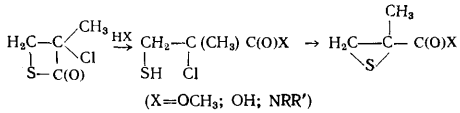
Historically the first example of these reactions is the syntheses of thiirans by Delepine's method [136–140], which were described soon after Staudinger's reports of the syntheses of tetra-arylthiirans. Delepine's method made it possible to obtain for the first time the lowest thiirans. The syntheses are based on the reaction of vicinal dithiocyanato- and halogenothiocyanato-alkanes with sodium sulphide:



Thiiran and 2-methylthiiran [136–141], tetramethylthiiran [142], thi-iranylalkanecarboxylic acids [143], and cyclohexeno[*b*]thiiran and its derivatives [144] were obtained by this method. The reactions are usually carried out in lower alcohols, aqueous alcohol, or water. The usual alkaline agents can be used instead of sodium sulphide [143,145]. Thi-iranylalkanecarboxylic acids are synthesised by treating the corresponding vicinal dithiocyanato-derivatives with sodium hydroxide [143]. The yield of the lowest thiirans in syntheses by Delepine's method is usually low owing to their polymerisation in the course of their formation. However, substances which are relatively stable under the conditions of the syntheses were obtained in virtually quantitative yields [142]. Delepine's method can be of practical interest for the conversion of higher olefins into thiirans in view of the availability of effective methods for the formation of vicinal chlorothiocyanato-alkenes.

The syntheses of thiirans from 2-halogenoalkanethiols, analogous to the halogenohydrin syntheses, were published for the first time in 1939. [146–148] A high yield of thiiran (up to 98%) was obtained under relatively mild conditions by adding alkali to chloroethanethiol, keeping the pH of the medium at about 7.5–9.5. Cyclohexeno[*b*]thiiran and cyclopenteno[*b*]thiiran (yield up to 80%), [100] as well as 2-mercaptomethylthiiran and 2-mercaptomethyl-2-methylthiiran [149] were obtained by this method under similar conditions.

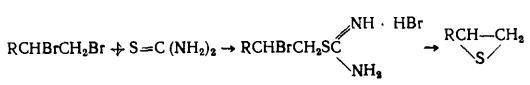
The reaction has been widely used by Knunyants and coworkers [150–156] in the syntheses of thioglycidic acids and their esters and amides. Numerous attempts to obtain these compounds by the reaction of glycidic acid derivatives with potassium thiocyanate or thiourea [104,157], by treating vicinal dithiolacetates with bases [158,159], and by the reaction of thioketones with chloroacetates [160] proved to be unsuccessful. The simplest examples of compounds of this series were obtained for the first time in good yields by treating the thiolactone of α-chloroisobutyric acid with ammonia and amines [150], with a mixture of alcohol and triethylamine [151], or with a dilute solution of alkali [152]. The reactions involves the preliminary opening of the thiolactone ring:



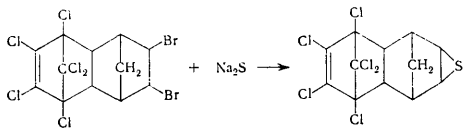
(X=OCH$_3$; OH; NRR')

Similar compounds have also been synthesised in yields up to 90% by mild alkaline treatment of derivatives of α-chloro-β-mercaptocarboxylic acids [153–156] obtained by the hydrolysis of the corresponding acyl derivatives.

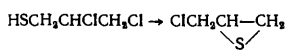
2-Halogenoalkylisothiuronium salts, formed by the reaction of vicinal dihalogenoalkanes with thiourea, react similarly to 2-halogenoalkanethiols [161]:



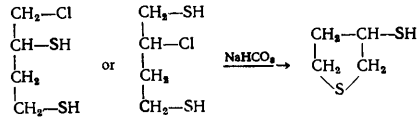
The conversion of vicinal dihalogenoalkanes into thiirans by reaction with sodium sulphide probably involves the formation of 2-halogenoalkanethiols [162]:



The mild conditions in the formation of the thiiran ring in the alkaline treatment of 2-halogenoalkanethiols make it possible to obtain thiirans containing highly reactive groups, for example 2-chloromethylthiiran [163]:

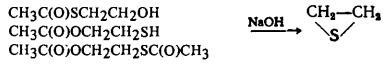


The reactions of 2-halogenoalkanethiols usually proceed unambiguously and the yield of products exceeds 70%. An anomalous reaction was observed only in the cyclisation of 3-chloro-1,4-dimercaptobutane and 4-chloro-1,3-dimercaptobutane [149], where 3-mercaptothiolan was isolated instead of the expected 2-(2-mercaptoethyl)thiiran:

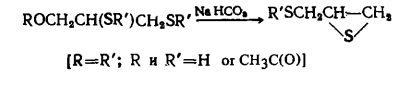


Thus the scope of the synthesis of thiirans from 2-halogenoalkanethiols is very great. The method makes it possible to obtain thiirans derived from strained cycloalkenes and thioglycidic acids, which are not formed in other synthesis.

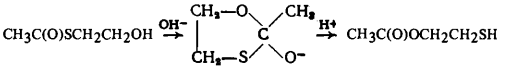
The first reports of the syntheses of thiirans from *O*-acetyl, *S*-acetyl, and *OS*-diacetyl derivatives of 2-mercaptoalkanols were published in 1949: [164-166]



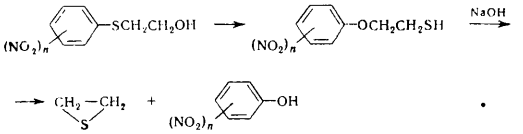
Partly or fully acylated 2,3-dimercaptopropanol was converted by this method into 2-mercaptomethylthiiran or into 2-acetylthiothiiran:



After analysing the above studies [164-166], Culvenor et al. [101] concluded that the formation of thiirans in these and similar instances known at the time is a consequence of the high capacity of 2-substituted thiols for isomerisation. They believe that the conversion of acylthioalkanols into thiirans is due to their marked ability to undergo anionotropic reactions:

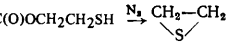


Hence it followed that a wide variety of mercaptoalkanol derivatives of the type $RSCH_2CH_2OH$, in which R is an electronegative group with a coordination-unsaturated central atom, can be converted into thiirans. This was in fact confirmed by Culvenor et al. [101] for the reaction of 2-hydroxyethyl nitrophenyl sulphides with bases:



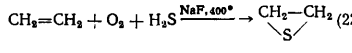
Culvenor's ideas stimulated extensive studies on the above reactions and were confirmed subsequently. Ethylene monothiocarbonates were decomposed by alkali [167], and thiiran could be synthesised in 70–80% yield by treating them with sodium methoxide. Cyclopenteno- and cyclohexeno-[*b*]thiirans were obtained in high yields from *trans*-2-acetylthiocyclopentyl acetate and *trans*-2-acetylthiocyclohexanol [168]. The same compounds were obtained [169] by the alkaline decomposition of *trans*-2-acetylthiocycloalkyl toluene-*p*-sulphonates. Doyle et al. [149] investigated the syntheses of thiirans from the triacetates of the dimercapto-derivatives of isobutyl, pentyl, hexyl, and decyl alcohols. Fully acylated 6-mercaptoglucose was converted into thiiran by treatment with sodium methoxide [170]. Similar compounds were also obtained by the alkaline decomposition of *S*-acyl-*O*-tosyl derivatives of carbohydrates [172-174]. The synthesis of thiirans from *O*-(2-mercaptoalkyl) esters of *O*-alkyl- and *O*-arylcarbonic and arylcarbamic acids and from *S*-(2-hydroxyalkyl)esters of *O*-alkylthiocarbonic and arylthiocarbamic acids has been patented [171]. The best yields of thiiran (67–80%) was obtained from the 2-mercaptoalkyl esters by treating the latter with sodium methoxide. When aqueous alkalis are used, the yield depends on the nature of the thiirans formed and varies from 25 to 85%.

A catalytic method for the conversion of 2-mercaptoalkyl acetates into thiirans was developed recently [175]:

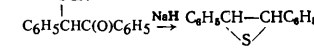


The esters are supplied to the reaction zone in a mixture with xylene in an atmosphere of nitrogen. The catalyst is based on aluminium with added sodium, iron, and silicon oxides. The degree of conversion of 2-mercaptoethyl acetate is 85% and the yield of thiiran reaches 70.5%.

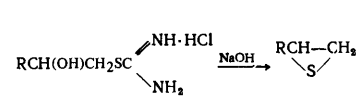
According to Harding et al. [165], 2-methylthiiran is obtained in low yield when 1,2-dimercaptopropane is treated with alkali. However, under the usual conditions 2-mercaptoalkanols are not converted into thiirans. A high-temperature alkaline cyclisation of monothioethylene glycol probably occurs when thiiran is obtained from ethylene, hydrogen sulphide, and oxygen [176]:



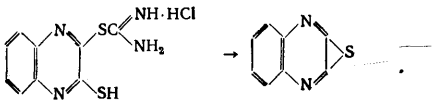
Like *S*-acyl derivatives of mercaptoalkanols, 2-thiocyanatoethanol [98] and 2-thiocyanatocyclohexanol [100] can be converted into thiirans. Decyl thiocyanate reacts similarly in the presence of sodium hydride [177] and a 2-hydroxylalkylisothiuronium salt:



or on treatment with alkali [178,179]:

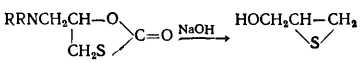


The hydrochloride of 3-isothiuronium-2-mercaptoquinoxaline is converted into thiiran even on crystallisation from dimethylformamide [180]:

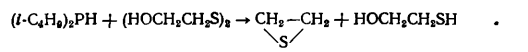


In the presence of bases thiirans are formed readily not only from thiocyanatoalkanols but also from their acyl derivatives [181].

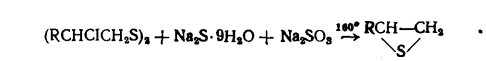
The derivatives of thiocyanatoalkanols, formed when cyclic alkylene carbonates are cleaved by alkali metal thiocyanates, undergo a spontaneous transformation into thiirans [182-184]. The mechanism of these reactions is analogous to that of the formation of thiirans from oxirans. The yield of thiirans reaches 65%. Cyclic alkylene monothiocarbonates [alkyl derivatives of 2-oxo-1,3-oxathiolan] are converted into thiirans in the presence of bases at 200°C. [185,186] Treatment of *NN*-dialkylaminomethyl derivatives of cyclic ethylene monothiocarbonates [2-oxo-1,3-oxathiolans] with alkali leads to the formation of 2-hydroxymethylthiiran [187]:



The last groups of reactions to be considered comprises those of 2-substituted polythio-compounds. The reduction of di-(2-hydroxyethyl) disulphide with di-isobutylphosphine results in the formation of thiiran together with ethylene monothioglycol [188]:

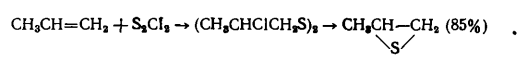


Substituted thiirans have been obtained by the reduction of di-(2-chloroalkyl) disulphides with a mixture of sodium sulphide and sulphite [189]:



The yield of 2-methylthiiran in this reaction reaches 77%.

A method has been patented for the synthesis of 2-methylthiiran from propene and sulphur monochloride [190]. Di-(2-chloropropyl) disulphide is first obtained in the presence of Friedel–Crafts catalysts and is then cyclised at 80–90°C over a mixture of sodium sulphide and carbonate:



A similar method was used to synthesise bisepithioalkanes from diene hydrocarbons [191]. The reduction of polymeric disulphides to thiirans was achieved in this case with the aid of aluminium in water.

Stereospecific syntheses of thiirans from alkenes have been achieved by the initial condensation of the latter with arenesulphenyl chlorides and the subsequent decomposition of the resulting aryl 2-chloroalkyl disulphides with sodamide or sodium sulphide [192,193]:

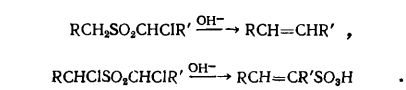
Cyclohexeno[*b*]thiiran, *cis*- and *trans*-2,3-dimethylthiiran [192], and thiirans derived from norbornenes [193] were obtained in this way in yields up to 70%.

Thiiran was also obtained in the decomposition of 2-chloroethyl 2-nitroethyl disulphide in the presence of potassium benzoate [194]:

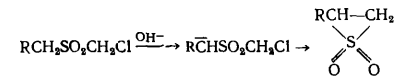
The above transformations of vicinal dithiocyanato- and halogenothiocyanato-alkanes, 2-halogenoalkanethiols, acyl derivatives of 2-mercaptoalkanols, 2-substituted dialkyl disulphides, and 1,2-dimercaptoalkanes into thiirans take place under conditions promoting the formation of 2-substituted thiolate anions. The anionotropic cyclisation of the latter takes place under mild or severe conditions depending on the nature of the substituent in the anion. The anionotropic formation of the thiiran ring takes place most readily in reactions of 2-halogenoalkanethiols.

4. ANIONOTROPIC REACTIONS OF DERIVATIVES OF α-HALOGENOSULPHIDES

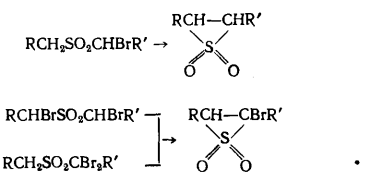
In 1940 Ramberg and Backlung [195] described a rearrangement of α-halogenosulphones accompanied by the elimination of sulphur dioxide and the formation of alkenes. αα-Dihalogenosulphones are converted into alkenyl sulphonates in these reactions:



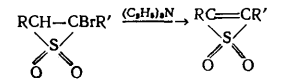
Somewhat later it was suggested on the basis of kinetic studies of these reactions [196] that the primary step in them is the elimination of a proton and cyclisation of the resulting anion with formation of a thiiran 1,1-dioxide:



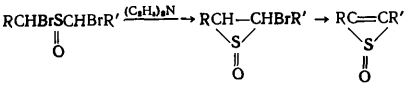
An experimental confirmation of the mechanism of the Ramberg–Backlung rearrangement was obtained by Neureiter and Bordwell [73,75], Paquette and coworkers [197-203], and Carpino and coworkers [204-206], who showed that, when a mixture of α-halogeno-, αα-dihalogeno-, and αα′-dihalogeno-sulphones is heated with triethylamine under mild conditions, the hydrogen halide is split off and thiiran 1,1-dioxides are formed:



Halogenothiiran 1,1-dioxides undergo further reactions under the above process conditions with formation of thiiren 1,1-dioxides:



α-Halogenosulphoxides undergo cyclisation reactions similar to those of α-halogenosulphones [206]:



Syntheses of thiirans from non-oxidised α-halogenosulphides under the conditions of anionotropic reactions have not been described.

5. THE FORMATION OF THIIRANS AS A RESULT OF CATIONOTROPIC REACTIONS OF ACYCLIC COMPOUNDS

Reactions involving cationotropic closure of thiiran rings have been little investigated. However, the data already available on these problems show that the practical applications of such syntheses are promising.

A method for the pyrolytic decomposition of 2,3-dimercaptopropanol to 2-mercaptomethylthiiran, which is of merely historical interest as the first attempt at the synthesis of thiirans by cationotropic reactions, was patented in 1948: [207]

$$HOCH_2CH(SH)CH_2SH \xrightarrow[-H_2O]{} HSCH_2CH\!-\!CH_2 \quad (S)$$

Better results were obtained in the pyrolysis of mercaptoalkanols in the presence of acids. Ethylene monothioglycol is converted into thiiran over potassium hydrogen sulphate at a temperature as low as 120°C. [208] The pyrolytic decomposition of ethylene monothioglycol in the monobutyl ether of triethylene glycol in the presence of t-dodecyl mercaptan [7,7-dimethyloctanethiol] and sulphuric acid leads to the formation of thiiran in 92.3% yield [209]. The initial cleavage of the C–OH bond with formation of the carbonium ion, which cyclises with elimination of a proton, is most likely in these reactions:

$$HOCH_2CH_2SH \xrightarrow[-HO^-]{} \overset{+}{C}H_2\!-\!CH_2SH \xrightarrow[-H^+]{} CH_2\!-\!CH_2 \quad (S)$$

This mechanism of the closure of the three-membered ring, involving the elimination of a cation, may be called cationotropic.

A few other reactions involving the formation of thiiran rings, which can be classified as cationotropic, are also known. Petrov and Sokol'skii [210] described the formation of 2-methylthiiran from chloromethyl ethyl sulphide in anhydrous hydrofluoric acid. Bearing in mind the ease of the heterolytic dissociation of the C–Cl bond in chloromethyl sulphides, the initial compound presumably dissociates with formation of a carbonium ion. The latter undergoes cationotropic cyclisation, facilitated by the $+I$ effect of the methyl group:

$$CH_3\!-\!CH_2\!-\!S\!-\!CH_2Cl \xrightarrow[-Cl^-]{} CH_3\!-\!\overset{H}{\underset{}{CH}}\!-\!\overset{+}{S}\!-\!CH_2 \xrightarrow[-H^+]{} CH_3\!-\!CH\!<\!\begin{matrix}CH_2\\S\end{matrix}$$

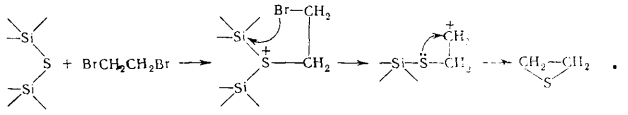
In this case cationotropic reactions do not involve the sulphur atom and the thiiran ring is formed from the carbon skeleton. There are similar reactions between $\alpha\alpha'$-dibromosulphoxides and phosphorus tris(dimethylamide) [211], which most probably involve the preliminary formation of an adduct of the quasiphosphonium type:

$$RCHBrSCHBrR' \;(\overset{\|}{O}) + [(CH_3)_2N]_3P \rightarrow RCH\!-\!CHR' \;(S,\overset{\|}{O}) + [(CH_3)_2N]_3PBr_2$$

The unusual reactions of compounds containing both sulphur and silicon with alkyl halides can be regarded as another example of processes of this kind [212]. On heating with dibromoethane, hexamethylcyclotrisilthiane decomposes by the reaction

$$[(CH_3)_2Si]_3S_3 + BrCH_2CH_2Br \rightarrow \begin{matrix}CH_2\!-\!CH_2\\ \diagdown S \diagup\end{matrix} + (CH_3)_2SiBr_2$$

The reactions in this system involving a preliminary alkylation of the sulphur atom can be attributed to the low strength of the Si–S bond and the high affinity between silicon and halogen atoms. The cationotropic transformations in this reaction involve the sulphur atom:



Reactions involving the cationotropic formation of episulphonium salts are of the same type. In a study by Gladshtein and Soborovskii [213] the methiodide of thiiran was obtained by treating the 2-thiocyanatoethyl ester of dimethylcarbamic acid with methyl iodide. The sulphonium salt formed initially in this reaction decomposes on heating to 100°C with decarboxylation and in the presence of methyl iodide undergoes further reactions:

$$(CH_3)_2NC(O)OCH_2CH_2SCN + CH_3I \rightarrow (CH_3)_2NC(O)OCH_2CH_2S\!-\!\underset{I}{\overset{CH_3}{CN}} \xrightarrow[-CO_2]{100^\circ}$$

$$\rightarrow (CH_3)_2NCH_2CH_2S\!-\!\underset{I}{\overset{CH_3}{CN}} \rightarrow CH_2\!-\!CH_2 \;(S^+\!-\!CH_3)\; I^- + (CH_3)_2NCN$$

Judging from the properties quoted by Gladshtein and Soborovskii [213], the structure $(CH_3)_2NCH_2CH_2SCH_3.ICN$ may be attributed to the decarboxylation product. Its conversion into the episulphonium salt is due to the cleavage of the C–N bond by iodine cyanide:

$$(CH_3)_2NCH_2CH_2SCH_3 + ICN \rightarrow \overset{+}{C}H_2\!-\!CH_2\!-\!\overset{+}{S}(CH_3) \rightarrow CH_2\!-\!CH_2\;(S^+\!-\!CH_3)$$

Knunyants and coworkers [214] described an elegant method for the preparation of episulphonium salts by the reaction of the amides of β-chloro-α-methylthioalkanecarboxylic acids with silver toluene-p-sulphonate. The reactions take place readily in solution in acetonitrile:

$$ClCRR'CR''C(O)NHR''' \rightarrow RR'C\!-\!CR''C(O)NHR'''\;(S^+\!-\!CH_3)$$
$$\quad\quad SCH_3$$

They proceed via a stage involving the formation of a carbonium ion, which rearranges to the sulphonium ion.

The above examples demonstrate the ready formation of thiiran rings by cationotropic reactions of 2-substituted thiol derivatives. The cationotropic closure of the thiiran ring can be achieved by the formation of the two-carbon skeleton or the C–S bond of the ring.

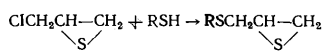
6. THE REACTIONS OF THIIRANS WITH RETENTION OF THE THIIRAN RING

There have been only a few syntheses of thiirans by this procedure. It has been shown in a patent [215] and in another report [113] that 2-acylthiomethylthiirans can be obtained by the selective acylation of 2-mercaptomethylthiiran:

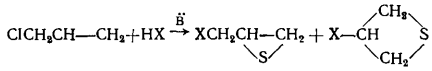
$$HSCH_2CH\!-\!CH_2\;(S) \xrightarrow{(CH_3CO)_2O} CH_3C(O)SCH_2CH\!-\!CH_2\;(S)$$

The electrophilic opening of the thiiran ring by acid anhydrides and chlorides takes place under more severe conditions, which makes it possible to obtain high yields of products formed by the acylation of the mercapto-group.

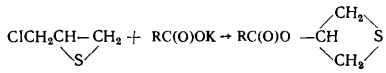
A wide variety of 2-methylthiiran derivatives have also been obtained by the nucleophilic substitution of the halogen atom in 2-halogenomethylthiirans. Unambiguous reactions occur only when 2-chloromethylthiiran reacts with thiophenols [216-219] and aliphatic thiols [220-223]. 2-Alkyl(aryl)methylthiirans are usually synthesised in aqueous media, using sodium and potassium hydroxides as the condensing agents:



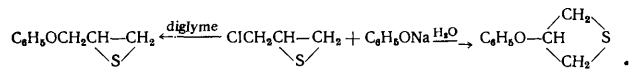
The reactions of 2-halogenomethylthiirans with phenols, alcohols, carboxylic acids, thiolocarboxylic acids, and *OO*-dialkylphosphorodithiolic acids are accompanied by side reactions as a result of the thiiran–thietan rearrangement:



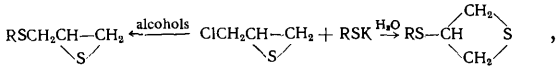
Under certain conditions, the side reaction can predominate and may even be the only one occurring. For example, the reaction of 2-chloromethylthiiran with potassium acetate in acetic acid results in the formation of 3-acetoxythietan and not a thiiran derivative [109]. 3-Acyloxythietans have also been obtained in a similar reaction of 2-chloromethylthiiran with sodium or potassium methacrylate, carbonate, chloroacetate, and benzoate in aqueous solutions [224,225]:



The mode of these reactions depends in many cases on the nature of the solvent employed. According to Sander [226], sodium phenoxides react with 2-chloromethylthiiran in diglyme to form 2-phenoxymethylthiirans, while in an aqueous medium the products are 3-aryloxythietans:



A similar behaviour was demonstrated by Arbuzov and coworkers [225,227-234] in reactions of *OO*-dialkylphosphorodithioate and thioacetate salts with 2-chloromethylthiiran. In aqueous solutions they observed the isomerisation of the thiiran ring to the thietan ring, while in anhydrous alcohols the main products were 2-acylthiomethylthiirans:

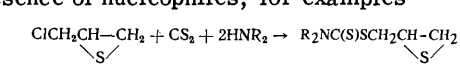


where R = CH_3CO or $(C_6H_5O)_2P(S)$. Similar results are presented in a patent [232].

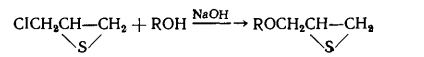
The course of the thiiran–thietan rearrangement depends to some extent also on the nature of the reactants employed. In the reaction between 2-chloromethylthiiran and thioacetates the thietan derivative is formed in a greater amount than in the reaction with *OO*-diethylphosphorodithioate [225]. As the electrophilic properties of the initial thiiran are enhanced, its tendency to isomerise in the reaction increases [228]. 2-Bromomethylthiiran is readily converted into a thietan derivative even under anhydrous conditions, while 2-acetoxymethylthiiran forms thiiran derivatives on reactions with salts of thiolic acids even in aqueous media.

The available information suggests that the thiiran–thietan rearrangement proceeds at the stage involving the formation of an ion pair. Unambiguous transformations with retention of the thiiran ring presuppose the creation of conditions for the formation of an ion pair, the recombination of which to an uncharged molecule takes place before the isomerisation of the cation. The loosening of the ion pair by the solvation shell promotes the isomerisation of the thiiran ring to the thietan ring.

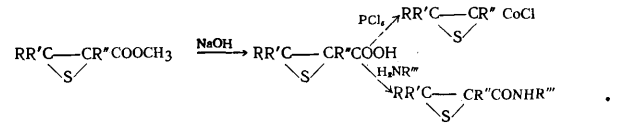
The three-membered ring of 2-chloromethylthiiran constitutes a weaker electrophilic centre than the carbon atom of the 2-methyl group. As a result, it is possible to obtain a wide variety of 2-methylthiiran derivatives from 2-chloromethylthiiran in complex systems and in the presence of nucleophiles, for examples [233,234]:



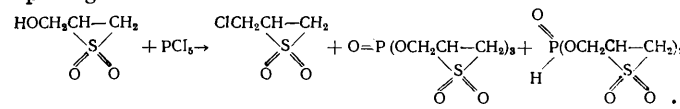
In the presence of aqueous alkali 2-chloromethylthiiran reacts with alcohols to form 2-alkoxymethylthiirans in yields up to 40% : [235]



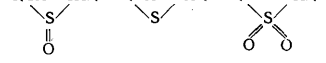
Despite the relatively high susceptibility of the thiiran ring to cleavage, thiirans could not be made to undergo a wide variety of reactions. Knunyants and coworkers [152,153] described reactions of thioglycidic acids and their derivatives which do not involve ring opening. They showed that methyl esters of epithioglycidic acids are hydrolysed under mild conditions by dilute alkalis. The thioglycidic acids obtained in this way could be converted under mild conditions into acid chlorides and amides:



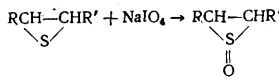
The reactions of 2-hydroxymethylthiiran 1,1-dioxide with phosphorus pentachloride also proceed without ring opening [187]:



The reactions of thiirans involving a change in the valence state of the sulphur atom constitute a special group. Mild oxidation of thiiran with hydrogen peroxide or perbenzoic acid leads to the formation of polyethylenesulphone [poly(thiiran 1,1-dioxide)] [71]. However, 2,3-diphenylthiiran is converted smoothly into thiiran 1-oxide or 1,1-dioxide in the presence of hydrogen peroxide or 3-chlorobenzoic acid [177,211]:



Thiiran 1-oxides and their homologues are obtained in high yields only on mild oxidation with sodium periodate in methanol [236]:



Thus the possibility in principle of the synthesis of thiiran compounds by reactions involving the substituents at the carbon atoms of the thiiran ring and the oxidation of the sulphur atom has now been established.

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The available data on the chemistry of thiirans are much less extensive than those for their nitrogen- and oxygen-containing heteroanalogues. However, the number of reactions leading to the closure of thiiran rings which have now been investigated is not less then the number of tested methods for the synthesis of oxiran, aziridine, and their homologues.

The available information about the syntheses of thiirans embraces virtually all possible types of methods for the homolytic and heterolytic formation of ring *endo*-bonds. Syntheses of thiirans involving the formation of their two-carbon skeleton via a homolytic mechanism and also via anionotropic and cationotropic cyclisation have been described. Methods based on the homolytic, anionotropic, and cationotropic closure of thiiran rings at the C–S bond have been widely investigated.

Numerous procedures for the preparation of thiirans are formally similar to the syntheses of aziridines and oxirans. For example reactions involving the anionotropic closure of thiiran rings at the C–S bond resemble the Gabriel–Wenker syntheses of aziridines and the chlorohydrin syntheses of oxiran and its homologues. Also similar are the methods for the synthesis of *N*-, *O*-, and *S*-heteroanalogues of cyclopropane based on the condensation of imines, carbonyl compounds, and thiocarbonyl compounds with carbenes, the pyrolysis of nitrogen-containing heterocyclic compounds, and cationotropic transformations of acyclic compounds. Thiirans are formed more readily in such reactions than oxirans and aziridines and the reactions themselves are more general. This is undoubtedly because of the smaller strain in thiiran rings and the characteristics of the electronic structure and behaviour of the sulphur atom.

The greater ease of formation of thiiran rings on energy grounds compared with oxirans is clearly shown in the reactions of derivatives of 2-mercaptoalkanols. The formation of three-membered heterocycles from ethylene carbonate and monothiocarbonate [2-oxo-1,3-dioxolan and 2-oxo-1,3-oxathiolan] takes place under virtually identical conditions (200°C). In the latter case the only product is thiiran. Thiiran and not oxiran is also formed from 2-mercaptoethanol and its acyl derivatives under the conditions of the anionotropic and cationotropic ring closure.

The methods for the synthesis of thiirans discussed in the review suggest a great scope for the synthesis of these compounds from simple readily available substances. From this point of view, there is no doubt that further development of thiiran chemistry can serve as one of the rational ways of solving problems which are at present important, namely that of the utilisation of sulphur and its simple compounds. On the other hand, the great synthetic possibilities in the series of thiiran compounds lead to good prospects for theoretical research. It is sufficient to mention that the discovery of the formation of thiiran compounds containing a ring formed at the double bonds of alkenes or in a chain of conjugated double bonds [26,180] is of general theoretical interest. The chemistry of thiirans with a halogen attached to the ring suggests ways for the investigation of the simplest heteroaromatic compounds with three-membered rings [206]. The syntheses and reactions of thiiran derivatives are of interest for modern stereochemistry.

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Functionally Substituted Cyclopropanes

L.A.Yanovskaya and V.A.Dombrovskii

Progress in the synthesis of functionally substituted cyclopropanes is surveyed together with certain of their properties as well as aspects of their structure and the transmission of electronic effects through the cyclopropane ring. A list of 225 references is included.

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I. INTRODUCTION

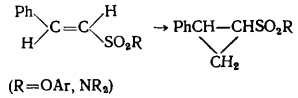
Functionally substituted cyclopropanes are of considerable interest. Firstly, they are fairly widely distributed in Nature. Examples are well known insecticides present in pyrethrum (*Chrysanthemum cinerariaefolium* Vis.), which are chrysanthemic esters and pyrethrolone or cinerolone ethers; and *cis*- and *trans*-isomers of 2-chloro-3-non-7'-ene-1', 3', 5'-triynylcyclopropylmethyl acetate have recently been detected[1] in *Centaurea ruthenica* Lam. The attractant of the American cockroach *Periplaneta americana* is also a cyclopropane derivative, for which the structure 2-isopropylidene-3,3-dimethylcyclopropyl propionate was suggested[2]. Furthermore, several cyclopropane derivatives, e.g. 2-(2,6,10,14-tetramethylpentadeca-1,5,9,13-tetraenyl)-3-(4,8,12-trimethyltrideca-3,7,11-trienyl)cyclopropylmethyl pyrophosphate (prephytoene pyrophosphate), are intermediates in the biosynthesis of steroids and carotenoids[3]. Several cyclopropane derivatives possess interesting physiological properties, like the above-mentioned derivatives of chrysanthemic acid, which have hitherto attracted the attention of chemists seeking new insecticides[4,5]. They exhibit not only insecticidal but also other types of activity. Thus several ketones have shown high anti-inflammatory activity[6].

The use of functionally substituted cyclopropanes as a convenient model for studying the ability of the cyclopropane ring to conjugate with the π-electrons of multiple bonds and examining the transmission of electronic effects through the ring has enabled a considerable approach to be made during recent years to solving this most complicated problem. Finally, several behavioural peculiarities of functional groups attached to a cyclopropane ring have been discovered recently.

The growing interest in functionally substituted cyclopropanes has led to the appearance of many publications on their synthesis, structure, and properties, but no systematic review of these results. The last survey of cyclopropane chemistry appeared in 1962 [7] and, of course, does not represent the present-day situation. The well known Houben—Weil work of reference[8] (1971) deals with methods for synthesising a cyclopropane ring irrespective of their possible use to obtain particular functional derivatives. We have therefore considered it useful to examine the most important papers on the synthesis, properties, and theoretical aspects of the chemistry of functionally substituted cyclopropanes which appeared between 1962 and 1973, referring to earlier work only in cases of extreme necessity.

II. SYNTHESIS OF FUNCTIONALLY SUBSTITUTED CYCLOPROPANES

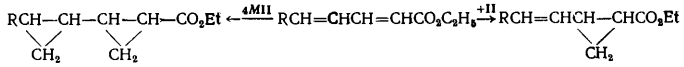
A most important advance in the synthesis of functionally substituted cyclopropanes during this period has been the practical introduction of the readily available sulphur ylides, which are able to transfer a methylene group to the polar double bonds of many unsaturated compounds to form cyclopropane derivatives. Examples are dimethylsulphonium methylide $(CH_3)_2\overset{+}{S}-\overline{C}H_2$ (I),[9-12] dimethylsulphoxonium methylide $(CH_3)_2\overset{+}{S}(O)-\overline{C}H_2$ (II),[13,14] aryldimethylaminosulphoxonium methylides $ArN(CH_3)_2.\overset{+}{S}(O)-\overline{C}H_2$ (III),[15,16] methyldialkylamino-oxosulphonium methylides $(CH_3).NAlk_2\overset{+}{S}(O)-\overline{C}H_2$ (IV),[17] etc. Among the suggested ylides, (II) and the highly reactive (IV) have been most widely used. Cyclopropanes can be synthesised also by means of functionally substituted sulphylides, such as dimethylsulphonium phenacylide $(CH_3)_2\overset{+}{S}-\overline{C}H.CO.C_6H_5$ (V),[18-20] methylphenylsulphonium phenacylide (VI),[21,22] dimethylsulphonium alkoxycarbonylmethylides $(CH_3)_2\overset{+}{S}-\overline{C}H.COOR$ (VII),[23-26] etc. Thus both mono- and poly-functional cyclopropanes can be synthesised by the use of sulphylides. Of course, not all the proposed sulphylides are synthetically equivalent. For example, the sphere of action of the methylide (I) is restricted to esters and amides of $\alpha\beta$-unsaturated carboxylic and sulphonic acids[27]. Thus ethyl cinnamate reacts with the ylide (I) to form ethyl *trans*-2-phenylcyclopropane carboxylate in 54% yield. Similarly, *trans*-2-phenylethylenesulphonic esters and amides are converted into those of *trans*-2-phenylcyclopropanesulphonic acid[27]:



(R=OAr, NR_2)

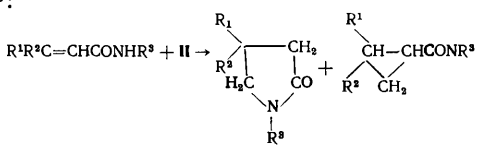
$\alpha\beta$-Unsaturated aldehydes and ketones react with (I) to form oxirans[11,12,14].

The methylide (II) is able to react also with esters of $\alpha\beta$-unsaturated mono- and di-carboxylic acids[10,28-31] to form high yields of esters of cyclopropane-mono- and -di-carboxylic acids. It is interesting that esters of diene acids react preferentially at the $\alpha\beta$-position. When a large excess of the methylide (II) is used, however, the diadduct can also be obtained[32]:



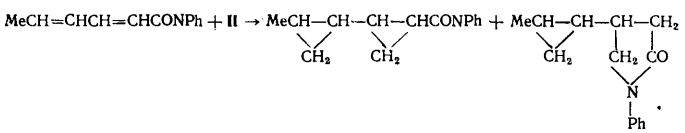
It must be emphasised that optically active 3-arylpropene-2-carboxylic esters yield optically active 2-arylcyclopropanecarboxylic esters on reaction with (II).[33] For example, (−)-menthyl and (+)-bornyl esters of cinnamic, *o*- and *p*-methoxycinnamic, and other acids react in this way.

Nitriles and amides of $\alpha\beta$-unsaturated acids also react with the methylide (II).[28,30,31,34] The former give nitriles of cyclopropanecarboxylic acids. Thus a 52% yield of 2-phenylcyclopropyl cyanide has been obtained from cinnamonitrile. Depending on their structure, amides will form amides of cyclopropanecarboxylic acids[35], pyrrolidones[30,34], or mixtures of an amide and a pyrrolidone[30,35]:

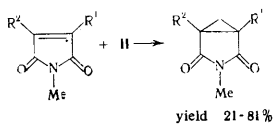


R^1	R^2	R^3	(VIII) Yield, %	(IX) Yield, %
H	H	H	50	0
Ph	H	H	0	40
Me	H	Ph	80	11

Sorbanilide forms a mixture[30,35]:

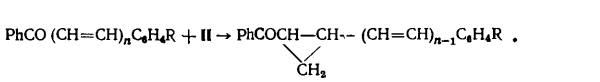


Reaction takes place between α-aryl-*N*-methylmaleimides and (II) without complications[34]:



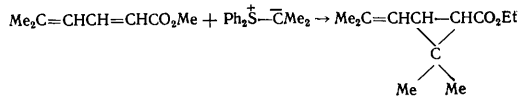
yield 21-81%

The reaction of conjugated ketones with the ylide (II), in contrast to that with (I), usually gives cyclopropyl ketones (aldehydes also form oxirans). Thus 5-methylhex-3-en-2-one and 3,6-dimethylhept-3-en-2-one are converted into the corresponding cyclopropyl ketones in 35–80% yields[30,31]. Alkyl aryl ketones—1-phenylbut-2-en-1-one[36] and chalcones[14,37]—react similarly, to give good yields of *trans*-aryl-2-benzoylcyclopropanes. In the case of vinylogues of chalcones reaction occurs at the double bond adjacent to the carbonyl group[37]:



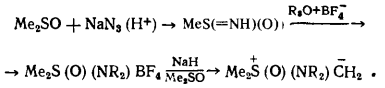
Use of the dideuterated methylide (II) enables aryl-2-benzoyl-3,3-dideuterocyclopropanes to be obtained[38,39].

The very reactive diphenylsulphonium isopropylide can be used for the synthesis of *gem*-dimethylcyclopropane systems having carbonyl functions[40]. A good yield of methyl (±)-*trans*-chrysanthemate has been obtained in this way[40]:



Methyl 2,2-dimethylcyclopropanecarboxylate (yield 71%) has been obtained similarly from methyl acrylate, dimethyl *cis*- and *trans*-3,3-dimethylcyclopropane-1,2-dicarboxylates (yields 75% and 82%) have been obtained from dimethyl maleate and fumarate respectively, etc.

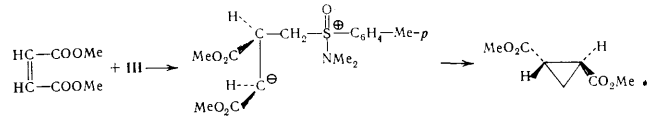
Use of the ylides (III) (Ar = C_6H_5) [15,16] and especially (VI) [17,41] has been recommended during recent years for the synthesis of functionally substituted cyclopropanes. These are readily accessible reagents, formed from dimethyl sulphoxide:



Cyclopropanes are easily formed by means of (III) and (IV) from cinnamic esters, mesityl oxide, benzylidenacetophenone, cyclohexenone, cinnamonitrile, phenyl styryl sulphone, etc. in yields of 50–98%. However, the main reaction product obtained from acrylo-*p*-toluidide is *N*-*p*-tolylpyrrolid-2-one.[30]

Use of the optically active (*R*)(−)-dimethylamino-oxo-*p*-tolylsulphonium methylide enables optically active cyclopropanes to be obtained in a quite high degree of optical purity. Thus the reaction of this ylide with methyl cinnamate gives methyl *trans*-(1*S*, 2*S*)-(+)-2-phenylcyclopropanecarboxylate in 76% yield with 30.4% optical purity[42].

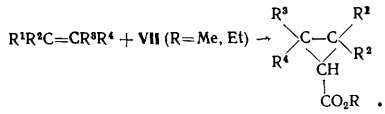
The reaction with sulphylides involves the intermediate formation of a betaine, which is confirmed by the formation of a single product—dimethyl *trans*-(1*S*, 2*S*)-cyclopropane-1,2-dicarboxylate (yield 50%, optical purity 17.8%)—on addition of the optically active ylide (III) (R = *p*-$CH_3C_6H_4$) to dimethyl maleate:



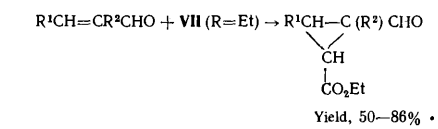
Formation of a *trans*-isomer from an initial *cis*-compound might have been explained by rotation about the single bond in the intermediate betaine, provided that formation of the latter was reversible. However, the above ylide (III) is able to isomerise dimethyl maleate into dimethyl fumarate[42].

Among the functionally substituted ylides (V)–(VII) the ethoxycarbonylide (VII) has found most extensive application during recent years, and provides an easy route to polyfunctionally substituted cyclopropanes. The ylide (VII) (R = C_2H_5) reacts readily with $\alpha\beta$-unsaturated esters (acrylic, methacrylic, crotonic, etc.), $\alpha\beta$-unsaturated ketones (methyl vinyl ketone, mesityl oxide), and nitriles (acrylonitrile) to form 45–90% yields of the corresponding

cyclopropanes when the reaction is conducted in an aprotic solvent (acetone, benzene, dichloromethane) at 45—80°C:[23-25,43]



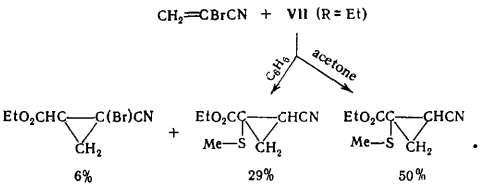
A most interesting feature of this ylide (VII) is that it reacts with $\alpha\beta$-unsaturated aldehydes, not at the carbonyl group like all other sulphylides, but at the double bond to form aldehyde derivatives of cyclopropane:



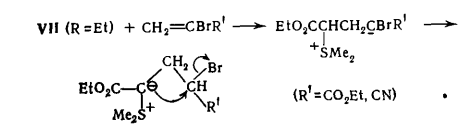
Yield, 50—86%.

Only acylic derivatives are obtained when the reaction is conducted in alcohol[44].

It is interesting that reaction of the ethoxycarbonylide (VII) with 2-bromoethyl acrylate in benzene forms a mixture of diethyl 1-bromocyclopropane-1,2-dicarboxylate and 1-methylthiocyclopropane-1,2-dicarboxylate (yields 36% and 25%), whereas in acetone only the latter product is formed in 52% yield. Reaction with α-bromoacrylonitrile occurs similarly:

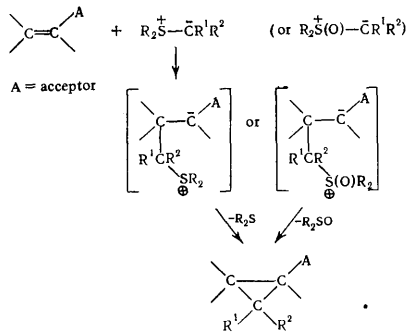


This can be explained by nucleophilic displacement in the intermediate betaine in polar solvents[24]:



The ylide (VI) reacts similarly to **VII** with $\alpha\beta$-unsaturated esters and ketones[21,22]. 1,2-Dibenzoyl-3-phenylcyclopropane (yield 77%) and 1,2,3-tribenzoylcyclopropane have been obtained by its use[20].

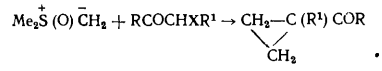
Methylene transfer is usually regarded as nucleophilic addition of the sulphylide at the polar double bond followed by elimination of a sulphide or a sulphoxide:



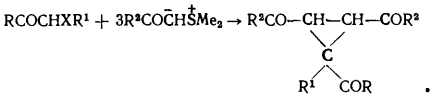
Transfer involving formation of a carbene is possible in certain special cases, e.g. in the decomposition of benzyldiphenylsulphonium tetrafluoroborate by the action of n-butyl-lithium in the presence of acenaphthylene in oxolan at −40°C with the formation of an isomer of 2-phenylphenalene[45], in the thermal decomposition of phenacyldimethylsulphonium bromide in the presence of cyclohexene with the formation of 7-benzoylbicyclo[4,1,0]heptane[18], and in the thermal decomposition of dimethylsulphonium aroylylides to 1,2,3-triaroylcyclopropanes[46].

In most cases transfer of the methylene group of sulphylides occurs stereospecifically with exclusive formation of *trans*-isomers[28,32,36-39,47]. Sometimes, however, e.g. in the reaction of the ylides (IV) with cinnamonitrile, a mixture of *cis*- and *trans*-isomers is formed (21% + 79%).[17] Similarly, the action of the ylide (VII: R = C_2H_5) on methacrylaldehyde give a mixture of *cis*- and *trans*-isomers in the proportions 68:2, with acrylaldehyde and crotonaldehyde the mixture contained 17—18% of the *cis*-isomer, with methyl vinyl ketone 2%, ethyl acrylate 3%, and methyl acrylate 9%. Chalcone, however, gave a mixture of roughly equal quantities of *cis*- and *trans*-isomers[43].

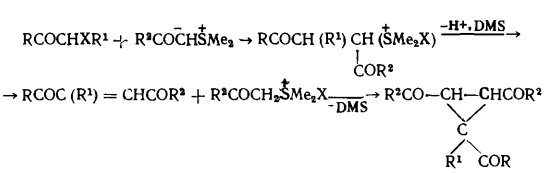
The use of sulphylides in the synthesis of cyclopropanes is not confined to reaction with activated double bonds. It was observed[22] in 1966 that the ylide (VI) reacts with bromoacetic ester in chloroform to give ethyl 2,3-dibenzoylcyclopropanecarboxylate, though in only 4,1% yield. It has since been suggested[48,49] that cyclopropyl ketones and cyclopropanecarboxylic esters can be synthesised by the action of the ylide (II) on α-halogenoketones (1-bromo-3,3-dimethylbutan-2-one, 2-chlorocyclohexanone, ω-bromoacetophenone, 2α-chlorotestosterone acetate, etc.) and on esters of α-halogenated acids (ethyl α-bromobutyrate, methyl α-bromo-α-phenylacetate):



The reaction is conducted with excess of the ylide in oxolan at −20° to −30°C, and the yields vary from 13% to 40%. The use of ylides of type (VI) enables trisubstituted cyclopropanes to be synthesised[50]:



Yields are 65—87% with bromo-ketones and phenacylides, and vary from 50% to 90% with alkoxycarbonylides. The probable reaction scheme



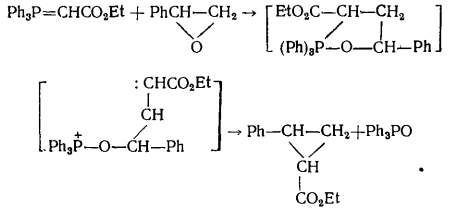
was suggested[50].

A further route for synthesising polyfunctional cyclopropanes by means of sulphylides is the reaction between mono- or di-substituted vinyldimethylsulphonium methyl sulphates $R^1.CH:CR.S(CH_3)_2CH_3SO_4$ and sodium derivatives of acids in alcoholic solution at 0°C:[51-53]

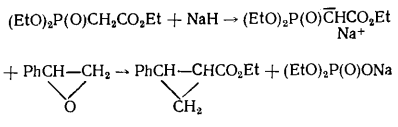
This method has been used to obtain 1,1-dicyano-2-phenylcyclopropane (yield 30%) from malononitrile, ethyl 1-cyano-2-phenylcyclopropanecarboxylate (60%) from

cyanoacetic ester, diethyl 2-phenylcyclopropane-1,1-dicarboxylate (60%) from malonic ester, etc. In every case only the *trans*-derivative was formed[53].

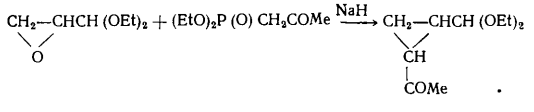
Phosphonium ylides also can be used for synthesising functionally substituted cyclopropanes, but to a limited extent. The most interesting method is the reaction of stable phosphonylides with epoxides[54-56], first described in 1962.[54] Thus ethyl triphenylphosphoranylidenacetate reacts with the α-oxides of oct-1-ene, cyclohexene, and styrene to form the corresponding cyclopropanecarboxylic esters and triphenylphosphine oxide. When styrene *l*-(−)-α-oxide is used, the optically active *trans*-cyclopropane is formed, though in low optical yield:



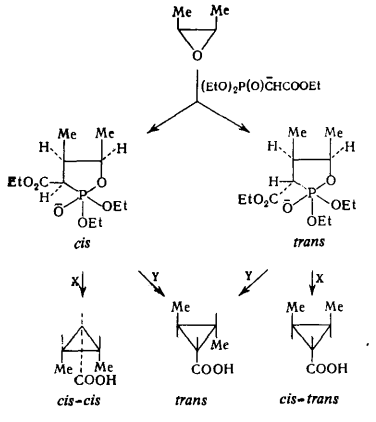
Phosphonate carbanions react similarly to phosphoranes with α-oxides of alkenes[57-61]. Thus ethyl diethoxyphosphinylacetate reacts with phenyloxiran in the presence of sodium hydride in diglyme at 85°C to form ethyl 2-phenylcyclopropanecarboxylate (yield 42%):[57]



A most interesting example is the synthesis of the acetal of 1-acetyl-2-formylcyclopropane in 60% yield[62] by the reaction of diethyl acetonylphosphonate with 2-diethoxymethyloxiran in the presence of sodium hydride in diglyme at 100—110°C:

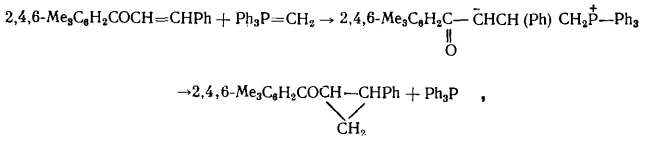


Fairly detailed investigations[54,58,63,64] led to the following mechanism for the reaction of phosphonates with oxides:



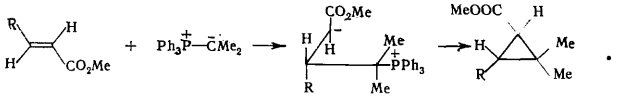
Such a scheme is supported by a study of the reaction of optically pure *trans*-(+)(2*R*, 3*R*)-2,3-dimethyloxiran and of the corresponding *cis*-isomer with ethyl diethoxyphosphinylacetate[64], to give after hydrolysis of the optically active *trans*-isomer a mixture of 90% of *trans*-(+)(2*S*, 3*S*)-2,3-dimethylcyclopropanecarboxylic acid, 6% of *cis*-2,*cis*-3-dimethylcyclopropanecarboxylic acid, and 1% of *cis*-2,*trans*-3-dimethylcyclopropanecarboxylic acid; the *cis*-isomer gave a mixture of 4% of racemic *trans*-2,3-dimethylcyclopropanecarboxylic acid, 6% of the *cis*,*cis*-isomer, and 90% of the *cis*,*trans*-isomer. Such proportions are explained by the relative quantities of intermediate cyclic products and(or) the relative possibility of X processes (direct decomposition of the intermediate ring by a synchronous mechanism or via a zwitterion) and Y processes (ring opening followed by attack from the rear); in the opening of the *cis*-oxide they undoubtedly represent steric control of the reaction after opening of the phosphonate ring.

Phosphylides can in some cases react also with $\alpha\beta$-unsaturated aldehydes and ketones to form cyclopropanes, not alkenes. Thus methylenetriphenylphosphorane reacts with mesityl α-styryl ketone[65] to form mesitoyl-2-phenylcyclopropane and triphenylphosphine:

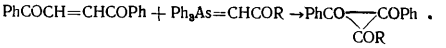


Steric hindrance by the mesityl group probably prevents reactions at the carbonyl group.

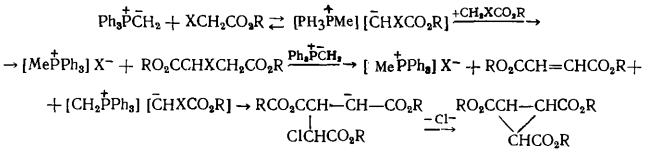
A convenient synthesis of *trans*-2,2-dimethylcyclopropanecarboxylic esters is based on the 1,4-addition of triphenylphosphonium isopropylide to *trans*-$\alpha\beta$-unsaturated esters followed by cyclisation of the intermediate with elimination of triphenylphosphine[66]:



Stable arsenic ylides react[67] with fumaric ester and *trans*-dibenzoylethylene to give good yields of the difficultly accessible 1,2,3-trisubstituted cyclopropanes in which all three substituents are electron-accepting:

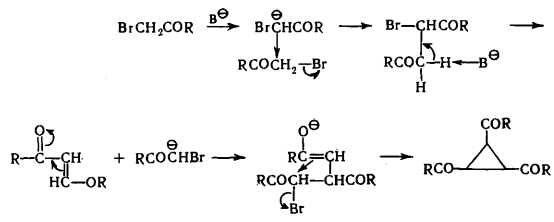


Certain phosphylides react with esters of α-halogenated acids to form trialkyl cyclopropane-1,2,3-tricarboxylates[68,69], for which the scheme

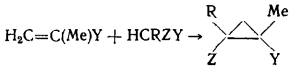


was suggested. The phosphylide thus acts as a base analogous to potassium t-butoxide, whose action on α-chloroacetamide gives *trans*-cyclopropanetricarboxamide[70]. Similar changes are produced also by the action

of lithium in liquid ammonia on ethyl bromoacetate[71] or of sodium hydride in Hexametapol on benzyl bromides or halogeno-acetic esters[72,73]:

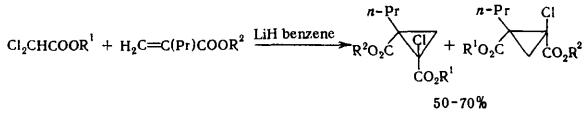


The formation of unsaturated compounds during the reaction is confirmed by the fact that ethyl bromoacetate reacts with ethyl acrylate or diethyl fumarate under the same conditions to form respectively diethyl cyclopropane-*trans*-1,2-dicarboxylate (yield 32%) and triethyl cyclopropane-*trans*-1,2,3-tricarboxylate (64%).[73] Thus the above reactions represent a particular case of the synthesis of cyclopropanes by the interaction of unsaturated compounds, activated by electron-accepting substituents (alkoxycarbonyl, cyano), with α-halogenated acids, ketones, or nitriles in the presence of hydrides or alkali-metal alkoxides[74-79]:



The isomer in which the electron-accepting groups activating the initial molecules are arranged in mutually *cis*-positions is often the principal or even the only product in this reaction. Thus methyl methacrylate reacts with methyl chloroacetate to give a 69—71% yield of a mixture of 93% of *cis*- and 7% of *trans*-dimethyl 1,2-dimethylcyclopropane-1,2-dicarboxylates; with methyl dichloroacetate only dimethyl *cis*-1-chloro-2-methylcyclopropane-1,2-dicarboxylate is obtained, in 74% yield. However, the reaction of methyl methacrylate with ethyl iodoacetate gives a 21% yield of a mixture of equal quantities of *cis*- and *trans*-isomers[74].

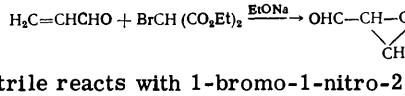
This method has recently undergone further development. Esters formed with different alcohols can be used, e.g. ethyl dichloroacetate and methyl α-propylacrylate, to give cyclopropanedicarboxylic esters with different alkyls[80]:



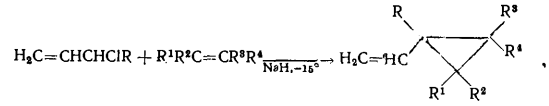
50-70%

The reaction is especially selective when an alcohol corresponding to the dichloroacetate is used to decompose the reaction mixture.

α-Unsaturated aldehydes also undergo this reaction. Thus acrylaldehyde and ethyl bromomalonate in the presence of sodium ethoxide give a 50% yield of diethyl 2-formylcyclopropane-1,1-dicarboxylate[81]:



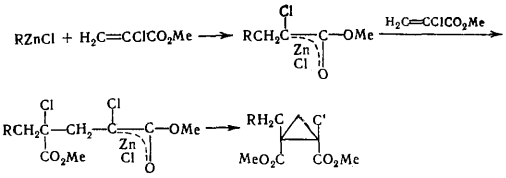
Malononitrile reacts with 1-bromo-1-nitro-2-R-ethylenes (R = C_2H_5, C_6H_5, p-$NO_2C_6H_4$) to form 1,1-dicyano-2-nitro-3-R-cyclopropanes[82]. Substituted vinylcyclopropanes can be obtained by applying the reaction to derivatives of 2-chlorobut-3-enoic acid[83]:



(R=CO_2Me, CN; R^4=COOMe, CN)

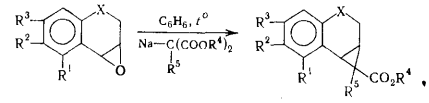
The stereochemistry of this reaction is controlled by the solvent: the formation of *cis*-isomers is favoured by solvents of low dielectric constant, and that of *trans*-isomers by solvents of high dielectric constant. In the reaction of 2-chlorobut-3-enonitrile with methyl acrylate in toluene, for example, methyl 2-cyano-2-vinylcyclopropanecarboxylate is formed with a total yield of 33%, comprising a 73 : 27 mixture of *cis*- and *trans*-isomers; when the reaction is conducted in Hexametapol the same cyclopropane is formed in 41% yield, comprising a 13 : 87 mixture.

A method proposed recently for synthesising cyclopropanedicarboxylic acids is based on the reaction of 2 moles of an α-chloroacrylate with 1 mole of an alkylzinc halide[84-87], and also enables *cis*-isomers to be obtained:



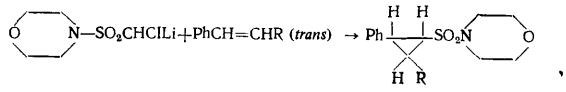
Partial asymmetric synthesis can be effected by the use of an optically active alkylzinc methoxide or a mixture of diethylzinc and an optically active alcohol (*l*-menthol).

Another new reaction for the formation of a cyclopropane ring consists in the nucleophilic opening of an oxide in the presence of a sodiomalonic ester in a non-polar medium[88,89]:



(X = CH_2, O) yield 37-64%

Addition of α-chloromorpholinosulphonylmethyl-lithium to an activated double bond to yield a cyclopropane[90] may be of interest:

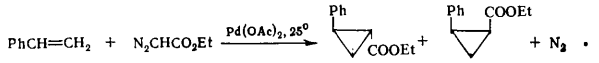


(R=SO_2Ph, CN, NO_2) yield 21-73%

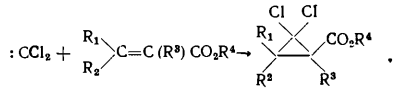
Such are the new synthetic methods which are of interest for the preparation of functionally substituted cyclopropanes. In addition, traditional methods have undergone further development, Firstly, unsaturated compounds have been treated with carbenes, which behave as electrophilic reagents[91]. Synthesis is based mainly on the addition of carbenes to functionally substituted alkenes. Functionally substituted carbenes—phenoxycarbene[92-96], alkoxycarbenes[97-100], selenocarbenes[10] sulphocarbenes[102,103], dicyanocarbenes[104-107], and several others—are seldom used in cyclopropane formation, with the exception of ethyl carbenecarboxylate[108-113].

As in previous years the main sources of carbenes have been diazo-compounds and polyhalogenated derivatives, with published methods of cyclopropane synthesis differing

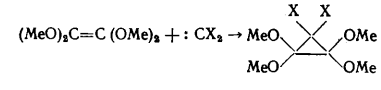
mainly in the mode of generation of the carbenes. It has been suggested that catalysts—copper powder[2,114,115], palladium acetate[116]—should be added to the diazo-compounds, in addition to the usual processes. Thus 2,4-dimethylpent-2-ene reacts with diazoacetic ester in the presence of copper powder to give ethyl 2-isopropyl-3,3-dimethylcyclopropanecarboxylate in 54% yield[2]. Similar methods of preparation have been used for *cis,cis*- and *trans,trans*-2-aryl-3-methylcyclopropanecarboxylic acids and esters[114], as well as for ethyl 2-methyl-3-propenylcyclopropanecarboxylates[115]. The corresponding cyclopropanes are formed by the action of diazoacetic ester on alkenes in the presence of palladium acetate in hexane[116]:



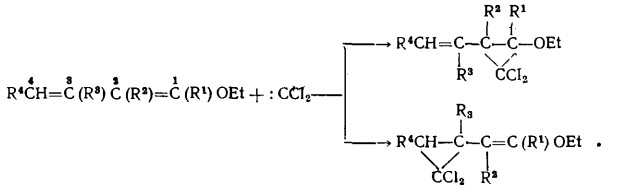
Dihalogenocarbenes have recently found fairly wide application for the synthesis of functionally substituted cyclopropanes. Besides traditional methods of generation (action of aqueous alkalis or alkoxides on polyhalogeno-derivatives) it has now been suggested that they should be generated by the action of aqueous caustic soda on polyhalogeno-derivatives in the presence of benzyltriethylammonium chloride as catalyst. The dichlorocarbene produced in this way adds e.g. at the double bond in $\alpha\beta$-unsaturated acids to form dichlorocyclopropanecarboxylic esters[117]:



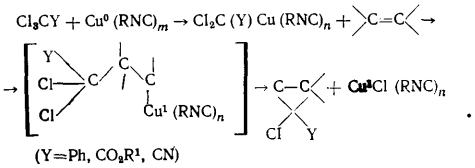
Interesting new examples have also been reported of the synthesis of functionally substituted cyclopropanes by means of dihalogenocarbenes. Thus dichlorocarbene adds at the double bond in acrylaldehyde diethyl acetal to form 1,1-dichloro-2-diethoxymethylcyclopropane in 33% yield[118]. An analogous reaction takes place with tetramethoxyethylene to give good yields of 1,1-dihalogeno-2,2,3,3-tetramethoxycyclopropanes[119]:



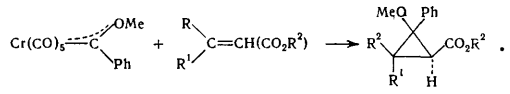
1-Ethoxybuta-1,3-dienes are also able to add dichlorocarbene. The reaction occurs non-stereospecifically, predominantly (67—100%) at the 3,4-double bond to give a mixture of substituted 1,1-dichloro-2-ethoxycyclopropanes (*trans*-1,2,*trans*-3,4 and *trans*-1,2,*cis*-3,4) in 20—40% yield[120]:



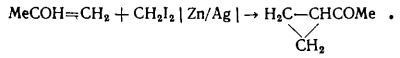
Polyhalogeno-derivatives can be used in other ways for the synthesis of cyclopropanes. Thus it has recently been suggested that alkenes having an electron-deficient double bond should be treated with copper carbenoid derivatives obtained by the reaction of trichloromethyl derivatives with copper and isocyanides[121,122]:



Functionally substituted cyclopropanes can be synthesised by the reaction of $\alpha\beta$-unsaturated esters with carbene complexes of transition-metal carbonyls. [123] For example, the complex of methoxy-phenylcarbene with chromium pentacarbonyl reacts stereospecifically when heated with *trans*-cinnamic, fumaric, and maleic esters to give 2-methoxy-2-phenylcyclopropane-mono- and -di-carboxylic esters:



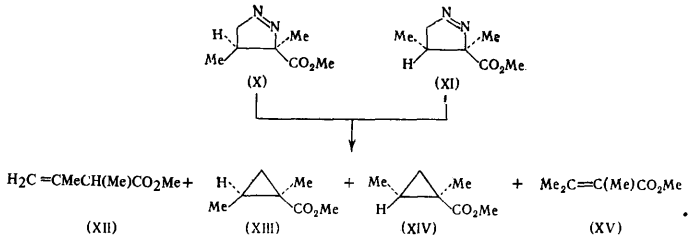
Several improvements have been introduced also into one of the oldest syntheses of cyclopropanes—the Simmons—Smith reaction. Thus an improved modification has recently been suggested in which the zinc—copper couple has been replaced by a zinc—silver couple, which enables functionally substituted cyclopropanes to be obtained in higher yields than by the original method. For example[124]



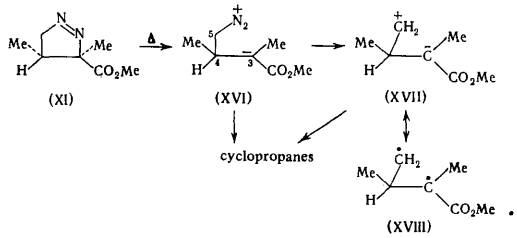
The Simmons—Smith reagent can be used[125] for the partial asymmetric synthesis of cyclopropanes from (−)-menthyl esters of $\alpha\beta$- and $\beta\gamma$-unsaturated carboxylic acids. Optically active *trans*-2-methylcyclopropanecarboxylic acid (yield 20—35%), *trans*-2′-methylcyclopropylacetic acid (54.5%), methyl *trans*-2-phenylcyclopropanecarboxylate (7—33%), and other derivatives have been obtained by this method[125].

The pyrolysis of pyrazolines is widely used to obtain cyclopropanes, and has been discussed in detail in several reviews[8,126,127]. We shall consider below only the most interesting new examples of the preparation of functionally substituted cyclopropanes by this method. Firstly, a detailed study by gas—liquid chromatography of the pyrolysis of methyl *cis*- and *trans*-3,4-dimethyl-Δ^1-pyrazoline-3-carboxylates showed[128] that, contrary to the widely held view, the configuration of the original molecule is in several cases not preserved in the thermal cleavage of Δ^1-pyrazolines, and the process is more complicated. For example, the pyrolysis of both *trans*- and *cis*-isomers (X) and (XI) gives a mixture of methyl 2,3-dimethylbut-3-enoate (XII), methyl *trans*-1,2-dimethylcyclopropanecarboxylate (XIII), methyl *cis*-1,2-dimethylcyclopropanecarboxylate (XIV), and methyl 2,3-dimethylbut-2-enoate

(XV), in the respective proportions 0.15 : 1.22 : 1.00 : 1.16 (X) and 0.24 : 0.70 : 1.00 : 3.73 (XI):



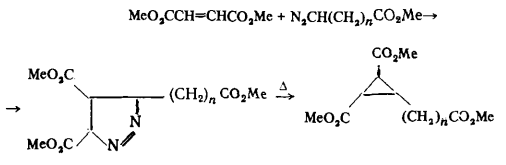
Since both mechanisms (ionic and biradical) suggested earlier for the thermal cleavage of Δ^1-pyrazolines involve preservation of the initial configuration, the non-stereospecificity observed in the above example was explained[128] on the assumption that the intermediate (XVI) is first formed, and is then converted with the loss of nitrogen into the intermediate (XVII), whose cyclisation yields the cyclopropanes:



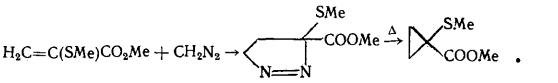
Loss of stereospecificity may result from free rotation about the $C_{(3)}-C_{(4)}$ bond, most probably in (XVI), since (XVII), which may resonate with the biradical (XVIII), would cyclise extremely rapidly.

Several new examples of the preparation primarily of cyclopropanemonocarboxylic acids and their derivatives by the pyrolysis of Δ^1-pyrazolines have been described during recent years[129-132]. Thus methyl 1-methylcyclopropanecarboxylate (yield 63%) has been prepared from methyl methacrylate via the corresponding Δ^1-pyrazoline; and a mixture of ethyl *cis*- and *trans*-2-phenylcyclopropanecarboxylates[133] from substituted styrenes and diazoacetic ester.

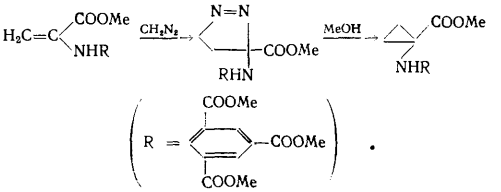
Furthermore, various cyclopropanes containing two carboxy-groups—in the ring or in the ring and in the side-chain—have been obtained by the thermal decomposition of Δ^1-pyrazolines from esters of unsaturated dicarboxylic acids[134-137]. The addition of ω-diazoalkanoic esters $N_2CH[CH_2]_nCOOCH_3$ ($n = 1-4$) to esters of unsaturated dicarboxylic acids is especially interesting, and leads to the formation of Δ^1-pyrazolinetricarboxylic acids, whose thermal decomposition gives cyclopropanetricarboxylic esters[138,139]:



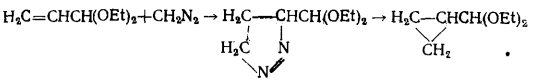
A few examples have also been reported of the preparation of cyclopropanecarboxylic acids containing other functional groups. Thus the Δ^1-pyrazoline obtained from methyl α-methylthio-acrylate and diazomethane is converted when heated (50°C) into methyl 1-methylthiocyclopropanecarboxylate[140]:



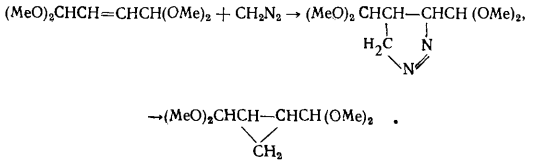
Similarly, boiling in methanol the Δ^1-pyrazoline from the tetramethyl ester of α-2, 4, 6-tricarboxyanilinoacrylic acid and diazomethane gives the tetramethyl ester of *N*-1′-carboxycyclopropylaniline-2, 4, 6-tricarboxylic acid[141,142]:



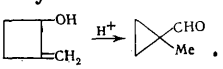
The Δ^1-pyrazoline from acrylaldehyde acetal and diazomethane is converted by pyrolysis at 400—450°C and 1 mm pressure into the acetal of cyclopropanaldehyde[143]:



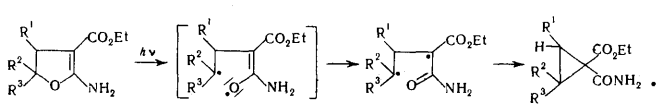
A method has been worked out[144] also for preparing 1, 2-bisdimethoxymethylcyclopropane[144] by the decomposition under similar conditions of 3, 4-bisdimethoxymethyl-Δ^1-pyrazoline, obtained from the easily accessible diacetal of fumaraldehyde and diazomethane, the yield reaching 93%:



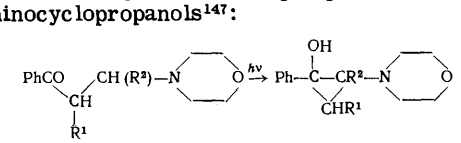
A few cases have been reported in which functionally substituted cyclopropanes have been formed in other ways. Thus heating 2-alkylidenecyclobutanols in a sealed tube or with 5% sulphuric acid converts them quantitatively into 1-alkylcyclopropanaldehydes[145]:



Irradiation of ethyl 2-amino-4, 5-dihydro-3-furoates in dioxan or oxolan in the presence of triphenylene or 2-naphthyl phenyl ketone as sensitiser yields a mixture of isomeric ethyl 1-carbamoylcyclopropanecarboxylates[146]:



Finally, the irradiation of certain 3-amino-ketones in dioxan in an atmosphere of nitrogen gives 80—95% yields of 2-aminocyclopropanols[147]:

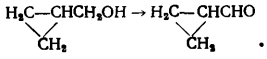


Thus almost any functional cyclopropane can be prepared by variations on the different methods available.

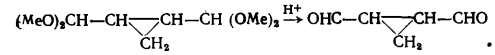
A fundamentally different method of obtaining functionally substituted cyclopropanes is to introduce functions into or to modify existing functional substituents in the cyclopropane ring, which presupposes a knowledge of the behaviour of various functional groups in the ring. Many data have been published on the reactions of cyclopropane rings involving rupture or change in the ring[7]. Considerably fewer publications have appeared on the reactions of functional groups attached directly to the cyclopropane ring. The following Section will be devoted to the most interesting new examples of such reactions.

III. SOME REACTIONS OF FUNCTIONALLY SUBSTITUTED CYCLOPROPANES

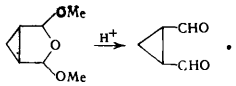
In most cases the behaviour of functional groups attached to a cyclopropane ring is almost identical with their behaviour in other classes of compounds. It has been shown during recent years, for example, that cyclopropylmethanol is oxidised to the aldehyde by hydrogen peroxide in the presence of iron(II) salts[148], aluminium isopropoxide[149], and also 1*N* aqueous ammonium cerium nitrate[150] (in the last case the yield of the aldehyde reaches 64%):



The acid hydrolysis of acetals of cyclopropane aldehydes goes in the usual way. Thus the diethyl acetal of cyclopropanaldehyde gives a 50% yield of the aldehyde when heated with 1*N* trichloroacetic acid[143]. The diethyl acetal of 2,2-dichlorocyclopropanaldehyde is hydrolysed, when heated with 12% sulphuric acid, to give a 50% yield of the corresponding aldehyde[118]. Finally, the hydrolysis of 1,2-bisdimethoxymethylcyclopropane gives, on heating with 6% phosphoric acid and removal of the resulting methanol by distillation, a 60% yield of cyclopropane-*trans*-1,2-dialdehyde[144] (the use of other acids or other conditions led to resinification and decomposition of the final hydrolysis product):



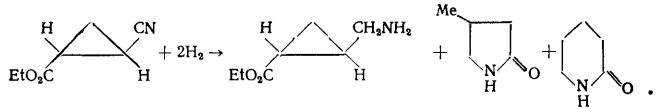
Hydrolysis of 2,4-dimethoxy-3-oxabicyclo[3,1,0]hexane even yielded the very unstable cyclopropane-*cis*-1,2-dialdehyde[151,152]:



Cyclopropyl cyanide undergoes fairly smooth reduction to cyclopropanaldehyde by the action of lithium hydrotriethoxyaluminate[153] or lithium hydrotri-n-butoxyaluminate[153]; and amides of cyclopropanecarboxylic acids, e.g. the ethylenamide[154] and the dimethylamide[155], are reduced quite smoothly by lithium tetrahydroaluminate, dihydrodiethoxyaluminate, or hydrotriethoxyaluminate. Yields of the aldehyde reach 20–60%, but, since it reacts under alkaline conditions, it can generally be isolated only as the 2,4-dinitrophenylhydrazine.

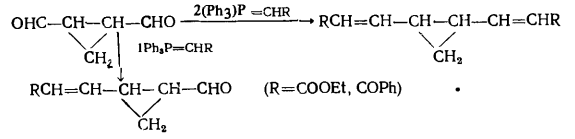
Cyclopropanecarbonyl chloride is reduced by lithium dihydrodi-t-butoxyaluminate to the aldehyde[154] (isolated only as the 2,4-dinitrophenylhydrazone). Similarly, Rosenmund reduction of cyclopropane-1,2-dicarbonyl dichloride gave cyclopropane-1,2-dialdehyde[156] (which also could be isolated only as the 2,4-dinitrophenylhydrazone).

The cyclopropane ring is preserved when ethyl *trans*-2-cyanocyclopropanecarboxylate undergoes catalytic reduction over Raney nickel under 50 atm at 35–37°C to ethyl 2-aminomethylcyclopropanecarboxylate[157]:



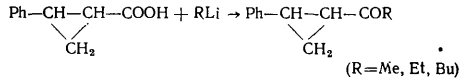
Boron hydride complexes reduce *N*-alkylidenecyclopropylamines only at the alkylidene group to the corresponding *N*-substituted cyclopropylamines in 70–90% yields[158].

Condensation of *trans*- and *cis*-2-phenylcyclopropanaldehydes goes normally with the sodium derivatives of phosphonacetic ester or benzylphosphonate to form ethyl *trans*- and *cis*-β-2-phenylcyclopropyl-α-R-acrylates (yield 50–60%).[159] Similarly, the condensation of dimethyl 2-formylcyclopropane-1,1-dicarboxylate with dimethyl 2-oxoheptylphosphonate gives a 70% yield of the αβ-unsaturated ketone[160]. Cyclopropane-1,2-dialdehyde also reacts with phosphonacetic ester, giving a 50% yield of diethyl cyclopropane-1,2-bis-α-R-β-acrylate[144]. Phosphonacetophenone and phosphonacetonitrile do not react with cyclopropane-1,2-dialdehyde under these conditions. The dialdehyde reacts normally under the conditions of the Wittig reaction, being converted by ethyl triphenylphosphoranylidenacetate and by phenyl triphenylphosphoranylidenemethyl ketone into products in which one or both aldehyde groups have reacted depending on the proportions of the reactants (yields 33–45%).[144]

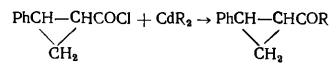


It is interesting that the condensation of phosphonacetic ester with dibenzoylcyclopropane in the presence of sodium hydride involves only one of the carbonyl groups even in the presence of excess of the reagent, and gives ethyl β-2-benzoylcyclopropylcinnamate[156].

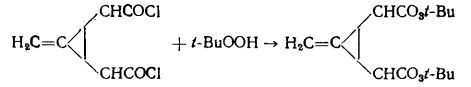
Treatment of the stereoisomeric 2-phenylcyclopropanecarboxylic acids with an alkyl-lithium under ordinary conditions gave the cyclopropyl ketones[161]:



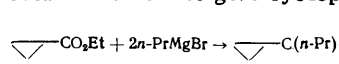
A dialkylcadmium converts cyclopropanecarbonyl chlorides also into ketones[161]:



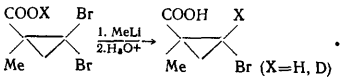
It is interesting that the action of t-butyl hydroperoxide on 3-methylenecyclopropane-1,2-dicarbonyl dichloride in pyridine gives a 70% yield of the di-t-butyl bisperoxycarboxylate[162]:



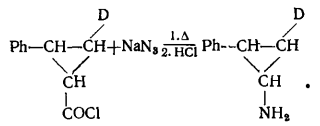
Ethyl cyclopropanecarboxylate reacts normally with *n*-propylmagnesium bromide to give cyclopropyldipropylmethanol[163]:



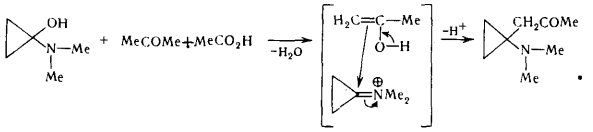
It is interesting that methyl-lithium causes stereoselective reduction of the bromine atom in the *cis*-position relative to the carboxyl in 2,2-dibromo-1-methylcyclopropanecarboxylic acid[164]:



Azides of stereoisomeric 2-deutero-3-phenylcyclopropanecarboxylic acids undergo the usual rearrangement to amines when heated[165]:

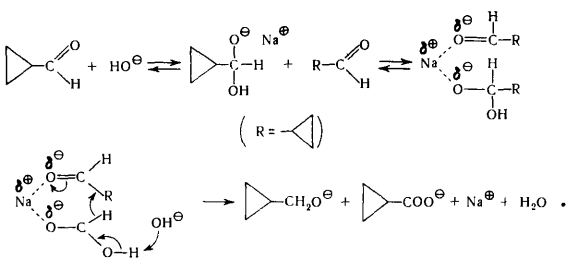


A Mannich base is obtained when 1-dimethylaminocyclopropanol is heated with acetone and acetic acid (at 65°C for 20 h):[166]



Acid hydrolysis of α-cyclopropyl-β-methoxystyrene goes normally to α-cyclopropylphenylacetaldehyde, which condenses in the usual way with but-3-en-2-one to give 4-cyclopropyl-4-phenylcyclohex-2-enone[167].

It has recently been shown that cyclopropanaldehyde, which contains an α-hydrogen atom, undergoes not an aldol condensation but the Cannizzaro reaction on treatment with aqueous alkali, with the formation of cyclopropylmethanol and cyclopropanecarboxylic acid. This is a second-order reaction with respect to aldehyde and alkali, and exhibits a small positive salt effect. Together with the absence of a deuterated cyclopropylmethanol when the reaction is conducted in heavy water, this suggests the reaction mechanism[168]



It is interesting that cyclobutanaldehyde forms aldol condensation products when treated with aqueous alkali[169].

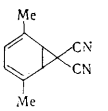
Thus functionally substituted cyclopropanes exhibit not only trivial behaviour but also unusual reactions, perhaps a consequence of structural peculiarities of the cyclopropane ring. The next Section will deal with current views on the structure of this ring system.

IV. STRUCTURE AND TRANSMISSION OF ELECTRONIC EFFECTS THROUGH THE CYCLOPROPANE RING

Cyclopropane is formally a saturated compound, in which the carbon atoms would have been in a state of sp^3 hybridisation. However, the angles between the carbon atoms in the cyclopropane ring differ markedly from those in saturated compounds. Two principal theories of the electronic structure of cyclopropane have been advanced, and examined in detail in a review[7]. According to Walsh[170] a carbon atom in cyclopropane is in a state of sp^2 hybridisation. Two sp^2 orbitals of each carbon atom form bonds with s orbitals of hydrogen. The remaining six electrons (two from each carbon atom) are involved in bond formation between the carbon atoms, of which four electrons belong to bonds formed by the overlapping of $2p$ orbitals, while the remaining two electrons form a three-centre orbital. This model explains the enhanced reactivity of the carbon–carbon bonds in cyclopropanes, evident in the easy rupture of the ring. The intensified p-character of the bonds in cyclopropane is confirmed by dipole moments and quadrupole magnetic resonance data obtained in a study of cyclopropyl chloride[171,172]. This model will also explain the ability of the cyclopropyl group to "conjugate" with π-electron systems, where "conjugation" implies the possibility of overlap of the three-centre orbital with π- and p-orbitals of a substituent (a vinyl group, a lone pair of electrons of an oxygen or a nitrogen atom, etc.)[173–175].

In the Coulson–Moffitt model[176] the carbon atoms are situated at the corners of an equilateral triangle, and hybridisation is such that two orbitals of any carbon form an angle of 104° in the plane of the ring. The carbon–carbon bonds are then curved (banana-shaped), the carbon atoms are in a state of $sp^{4,12}$ hybridisation, and the orbitals of the carbon–hydrogen bonds are in a state of $sp^{2,28}$ hybridisation[177]. The angle between the axes of the $sp^{4,12}$-hybridised orbitals is 104°.

The presence of curved bonds in cyclopropane is supported experimentally by the distribution of electron density in 7,7-dicyano-2,5-dimethylnorcaradiene



found by X-ray diffraction. The bending of the carbon–carbon bonds in the cyclopropane ring was shown to be ~20° (theoretically 22°). These results indicated also that the cyclopropane ring forms an angle of 73° with the cyclohexadiene plane[178].

Although the two models of cyclopropane are mathematically equivalent[179], the Coulson–Moffitt model permits certain predictions which cannot be made by means of the Walsh model. Furthermore, a model with curved bonds can be used to depict orbitals in those cyclopropane molecules which cannot be represented solely in terms of sp, sp^2, and sp^3 hybridisation.

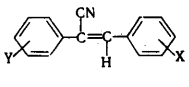
Various methods of quantum-chemical calculations have lately been used to study the electronic structure of cyclopropane[180–182]. Non-empirical calculations by the LCAO-MO self-consistent field method have established[183] that overlapping of the d-orbitals of the carbon atoms in the carbon–carbon bonds is possible, as well as the above two types, and should be taken into account in discussion of the hybridisation of the carbon atoms in the cyclopropane ring.

Calculations have shown that, in the ground state of cyclopropane, the highest electron density is concentrated on the carbon atoms, diminishes in the region between the hydrogen atoms attached to carbon, but is quite high between the carbon atoms along the carbon–carbon axis, and some charge is also concentrated at the centre of the ring. Thus the bonds retain a considerable p-character in the proposed model, which will explain the ability of the

cyclopropane ring to "conjugate" with π-electron systems.

Optimum conditions for interaction between the cyclopropane ring and the p-orbitals of an adjacent carbon atom in the side-chain are satisfied if the plane of the ring and the axes of the p-orbitals are parallel[177,184-189].

The possibility of electronic interactions between the cyclopropane ring and unsaturated groups and the transmission of the effect of substituents through the ring have been studied by many chemists[170,186-192]. An induction mechanism of transmission is evidently fully applicable to the cyclopropane ring. Hitherto, however, there has been no generally accepted view on the possibility of a mesomeric mechanism of transmission of electronic effects through the ring, i.e. on the possibility of conjugation between the cyclopropane ring and multiple bonds, and this problem remains a matter of controversy.



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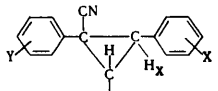

(XIX)

Table 1. Cyanide frequencies and reaction constants of series of cyanocyclopropanes (XIX) and cyanostilbenes (XX).

X	Y	Series (XX) ν_{CN}, cm^{-1}		Series (XIX) ν_{CN}, cm^{-1}	
p-Me_2N	H	2236.5	ρ=0.345	2207	ρ=0.250
p-Me_2N	p-Cl	2237		2209	
p-Me_2N	p-NO_2	2240		2212	
H	p-NO_2	2242	ρ=0.447	2220.5	ρ=0.104
p-NO_2	p-NO_2	2243		2226	
m-NO_2	p-NO_2	2243		226.5	
p-OCH_3	p-NO_2	2241		2218	

Table 2. Carbonyl frequencies (ν_{CO}, cm^{-1}) of p-R.C_6H_4.X.CO.C_6H_5 series in chloroform.

X	H	i-Pr	Me	F	Cl	Br	NO_2
—CH—CH \ / CH_2	1666	1668	1667	1668	1670	1668	1670
—CH=CH—	1665	1663	1662	1667	1666	1667	1670
No bridge	1660	1658	—	—	—	1660	—
—CH_2CH—	1685	—	1685	—	—	1687	—

Infrared spectroscopy, Raman spectra, nuclear magnetic resonance spectra, dipole moments, and pK_a values of acids have been used to study the interaction of a three-membered ring with adjacent unsaturated groups in the ground state. The effect of substitution on the infrared frequency of the functional group has been studied in greatest detail on 1,2-diphenylcyclopropyl cyanides, when the cyanide frequencies correlate with the α-constants of the substituents. However, the slope of the correlation graph is considerably smaller than for the corresponding series of cyanostilbenes. Furthermore, the CN frequencies in cyclopropanes are appreciably lower than that in benzyl cyanide (2256 cm^{-1}—Table 1).

Comparison of the carbonyl frequencies of 1-aryl-2-benzoylcyclopropanes and of substituted chalcones, benzophenones, and 1-aryl-2-benzoylethanes[37] (Table 2) shows that replacement of an ethylene unit by a cyclopropane ring or a vinylene fragment produces a large shift (~20 cm^{-1}) in the carbonyl frequencies, which confirms the ability of the cyclopropane ring to conjugate with the carbonyl group. However, the introduction of various *para*-substituents into the phenyl ring in 1-benzoyl-2-phenylcyclopropanes has little effect on the carbonyl frequency.

Table 3. Integral intensities of bands due to cyclopropanes and to unsaturated compounds.

Compound	Integral intensities of bands		
	C_6H_5, 1660 cm^{-1}	C=C, 1640 cm^{-1}	C=O, 1700 cm^{-1}
trans-1-Phenyl-2-vinylcyclopropane	1320	1250	–
1-Phenylbuta-1,3-diene	19600	48000	–
4-Phenylbut-1-ene	480	400	–
Ethyl *trans*-β-2-phenylcyclopropylacrylate	2900	9500	2700
Ethyl *cis*-β-2-phenylcyclopropylacrylate	1200	4500	1350
Ethyl 5-phenylpenta-2,4-dienoate	50500	16500	12000
Ethyl 3-methyl-5-phenylpent-2-enoate	590	2000	580

Raman spectroscopy was used to make very detailed studies[194,195] of the interaction of a cyclopropyl group with unsaturated side-chains. The ability of the ring to transmit the conjugation of attached groups was determined by examining the Raman spectra[196] of a series of 1-phenyl-2-R-vinylcyclopropanes and corresponding unsaturated or saturated compounds. Comparison of the integral intensities (Table 3) indicates that a three-carbon ring is able to conjugate with attached unsaturated groups and to transmit their influence provided that conformations most favourable for such conjugation are established, so that the π-orbitals of the substituent are able to overlap the Walsh three-centre orbital of the cyclopropane ring.

The proton magnetic resonance spectra of 1,2-diphenylcyclopropyl cyanides reveal[193] a correlation between the chemical shifts of the 2- and 3-hydrogen atoms and the constants of the substituents:

$$\nu(\text{Hz}) = K(0{,}4\sigma_I + 0{,}7\sigma_M) .$$

A correlation analysis established that the substituents affect the chemical shifts of the protons mainly by a mesomeric mechanism.

A comparative study of the proton magnetic resonance spectra of *trans*-1-benzoyl-2,2-dideutero-3-R-phenylcyclopropanes, *trans*-2-benzoyl-3-R-phenyloxirans, and *cis*- and *trans*-2-benzoyl-1-cyclohexyl-3-R-phenylaziridines in deuterochloroform and in benzene showed that the differences between the chemical shifts in these two solvents correlated with the σ, σ^0, and σ^+ constants of the substituents. However, the best correlation is obtained by using the Swain F and R constants (the field-effect and resonance constants respectively). Values of 25.7, 23.3, and 13.4 were found for the reaction constants ρ of the cyclopropane, oxide, and ethylenimine rings

respectively. These results agree well with a study of the ^{19}F nuclear magnetic resonance spectra of series of compounds p-F.C_6H_4.X.C_6H_4.Y, which gave the values of ρ (the slope in ppm) −2.20, 0.84, −1.21, and −1.20 according as X was CH : CH, $CH_2.CH_2$, a cyclopropane ring, or an oxide ring. However, the substituent constants σ_1 and σ^0_R found for the cyclopropyl group in a ^{19}F-n.m.r. study of m- and p-fluorophenylcyclopropanes[200] were closely similar to those for alkyl substituents. Hence it was concluded that, in the ground state of the fluorocyclopropane molecule, the phenyl and cyclopropyl groups do not interact by a mesomeric mechanism.

Table 4. Dipole moments of ketones R.C_6H_4.X.CO.C_6H_5 (in benzene at 25°C).

R	No bridge	—CH=CH—	—CH—CH— (CH$_2$)		
	μexp	μexp	μexp	μcalc	μinter
H	2.99	3.07	2.45	2.90	−0.45
Cl	2.95	2.57	1.82	1.91	−0.01
Br	2.96	2.91	1.89	1.90	−0.01
NO_2	4.23	4.16	3.68	4.10	−0.42
m-NO_2	—		3.61	4.10	−0.49
MeO	—	3.60	2.97	2.80	0.17

The very small interaction moments $\mu_{inter} = \mu_{exp} - \mu_{calc}$ indicate (Table 4) absence of appreciable conjugation between the π-electron system of the p-R.C_6H_4 group and benzoyl in *trans*-1-benzoyl-2-p-R-phenylcyclopropanes. Comparison of the dipole moments of these cyclopropanes with those of corresponding benzophenones and chalcones (Table 4) shows that introduction of the cyclopropane ring lowers the dipole moments in comparison with benzophenones, and does not increase them, as with chalcones: i.e. cyclopropyl ketones are less polar than are benzophenones[201].

Finally, pK_a values were determined for a series of *para*-substituted *trans*-2-phenylcyclopropanecarboxylic, cinnamic, and β-phenylpropionic acids in dilute aqueous solution[202] and later in 50% ethanol[203] in order to assess the ability of the cyclopropane ring to transmit electronic effects, and a correlation analysis of the data was made. The results were contradictory. In aqueous solution the series of phenylcyclopropanecarboxylic acids and the series of phenylpropionic acids had closely similar reaction constants ρ (0.182 and 0.212 respectively; for the series of cinnamic acids ρ = 0.466), which indicates absence of interaction between the phenyl group and carboxyl through the cyclopropane ring. In alcoholic solution, however, an appreciable difference was observed between the reaction constants of the two series (0.473 and 0.344 respectively for the cyclopropane and phenylpropionic series): i.e. under these conditions the cyclopropane ring transmits electronic effects appreciably better than does an ethylene bridge. This discrepancy may be due to variation in the conformation of the compounds with the solvent. Indeed, it has been known for some time[204] that the degree of ionisation of stereoisomeric cyclopropanecarboxylic acids containing one, two, or three substituents in the ring depends to a greater extent on their spatial configuration than on the polar nature of the substituents.

It is clear from the above discussion that any conclusion on the ability of the cyclopropane ring to conjugate or to transmit effects in the ground state cannot be examined without qualification to all cyclopropane systems. Nevertheless, an inductive effect—not a mesomeric effect—predominates in the ground state in the majority of examples.

An analogy between the cyclopropane ring and the double bond can very often be traced in the excited state. The problem of the conjugation of substituents and of the transmission of their electronic effects through the cyclopropane ring in the excited state was studied quite widely by means of ultraviolet spectroscopy[200-214]. The main criterion of the possibility of conjugation between the cyclopropane ring and a substituent is a bathochromic shift and intensified absorption in comparison with model compounds not containing a cyclopropane ring.

Table 5. Wavelengths λ_{max} (nm in alcohol) in the compounds $C_2H_5O.CO.CH : CH.X.CH : CH.COOC_2H_5$ in comparison with $CH_3.CH : CH.COOC_2H_5$.

X	λ_{max}	ε
No bridge	264	30300
—CH=CH—	304	46800
C_6H_4	323	46200
—CH—CH— (CH$_2$)	252	22800
MeCH=CHCO$_2$Et	206	15520

Thus the sharp bathochromic shift (4—10 nm) in the electronic spectra of 1-aryl-2-benzoylcyclopropanes in comparison with 1-benzyol-2-phenylethane indicates interaction between the benzoyl chromophore and the cyclopropane ring. However, the nature of a substituent in the benzene ring has hardly any effect on the position of the maximum of the benzoyl chromophore[37]. The presence of a bathochromic shift in the electronic spectra of compounds of general type $C_2H_5O.CO.CH : CH.X.CH : CH.COOC_2H_5$ (Table 5) indicates quite definite interaction between chromophores separated by a cyclopropane ring[144]. Bathochromic shifts (5—29 nm) [211,212] have been observed also in the electronic absorption spectra of cyclopropylacrylic esters and corresponding models containing no cyclopropane ring. The introduction of substituents capable of conjugation into a benzene ring attached to a cyclopropane ring causes bathochromic shifts and some strengthening of absorption bands[193].

Variation from 0 to 90° in the orientation of the cyclopropane ring relative to the bisecting plane in a series on conformationally rigid p-nitrophenylcyclopropanes has little effect on the electronic interaction between the cyclopropyl group and the nitrophenyl or phenyl chromophore, according to a study of the electronic spectra of such compounds. This indicates that inductive effects play the main part in these series[215]. In an interesting example of the steric suppression of conjugation of the cyclopropane ring with double bonds[216] disturbance of the arrangement of the ring in the plane of the double bonds optimum for conjugation, on the introduction of methyl groups into the ring or into a side-chain, causes hypsochromic shifts in the electronic spectra of cyclopropylacrylic esters.

Comparison of the electronic spectra of stereoisomeric 1-phenyl-2-R-cyclopropanes (R = COOH, COR', $CONH_2$, NR'_2, CH : CH.COOH, or CH : $CH.COOC_2H_5$) with the spectra of monosubstituted cyclopropanes (phenylcyclopropane and β-cyclopropylcrotonic ester) indicates that the cyclopropane ring is able to transmit the effect of attached groups, but to a less extent than can be vinylene bridge. Differences in the spectra of ethyl *cis*- and *trans*-β-2-phenylcyclopropylacrylates can be explained by steric effects on the formation of a single conjugated system and linked with the relative orientation and the degree of overlap of the orbitals of the three-membered ring with the π-orbitals of neighbouring unsaturated groups. Such overlapping is evidently weaker in the *cis*-isomers, which is probably responsible for the hypsochromic displacement of the longer-wavelength absorption band and its diminished intensity in comparison with the *trans*-isomers[217].

In contrast to earlier results[218] indicating absence of appreciable conjugation between a cyclopropyl ring and substituents (study of the electronic and circular dichroism spectra of *trans*-2-phenylcyclopropanecarboxylic acid), a subsequent careful investigation[219] of the ultraviolet and circular dichroism spectra of the same acid has revealed the presence of some electronic interaction between phenyl and carboxyl chromophores and the transmission of electronic effects through the cyclopropane ring.

Steric conditions necessary for maximum delocalisation of electrons in a system comprising cyclopropyl and an unsaturated group in an excited state were postulated by several workers[170,184,185,207,213,220]: (i) the π-bonds of the unsaturated group and the cyclopropane ring should be coplanar; and (ii) the plane containing the atoms of the unsaturated group should cut the three-membered ring along a bisecting line. However, study of conjugation effects in phenylcyclopropane derivatives with a fixed spatial arrangement of the phenyl group and the cyclopropane ring led to the conclusion that no preferred geometry exists for conjugation between them[209]. Examination of the electronic spectra of many cyclopropyl ketones indicated also considerable conjugation interaction between the three-membered ring and the unsaturated centre even when only one cyclic carbon–carbon bond was involved in conjugation[205]. Thus conjugation and the transmission of electronic effects through a cyclopropane ring in the excited state constitute an extremely complicated problem.

Table 6. Reaction constants ρ for $R.C_6H_4.X.COOC_2H_5$ (correlation analysis of alkaline hydrolysis constants).

X	ρ	X	ρ
$-CH_2-CH_2-$	0.591		0.812
trans-CH=CH-	1.314		
cis-CH=CH-	1.122		1.02

Relatively little study has been made of the transmission of the effect of substituents through the cyclopropane ring in a reactive state. Thus correlation analysis of the alkaline hydrolysis constants of ethyl *meta*- and *para*-substituted *trans*- and *cis*-2-phenylcyclopropanecarboxylates in 87.8% ethanol at 37°C enabled reaction constants to be determined for these series (Table 6) and the ability to transmit electronic effects in comparison with *cis*- and *trans*-cinnamic, β-phenylpropionic, and phenylpropiolic esters to be assessed as lying in the sequence[221]

$$CH_2.CH_2 < \textit{trans}\text{-}\Delta < \textit{cis}\text{-}\Delta < \textit{cis}\text{-}CH:CH < \textit{trans}\text{-}CH:CH < C:C.$$

Measurements of ionisation constants were used to assess the effect of two phenyl groups separated by a three-membered ring in 2,3-diphenylcyclopropanecarboxylic acids[222].

Correlation analysis of a kinetic study of the reaction of diphenyldiazomethane with *trans*-2-arylcyclopropanecarboxylic acids in toluene at 35–65°C established that use of the σ-constants of substituents in the aromatic ring gives the best correlation of the esterification rate constants. The transmission factor π' for the three-carbon ring was also calculated[223]. The result (0.40) was close to the value π' = 0.33 calculated from the p*K* of cyclopropanecarboxylic acids[224]. The data indicate that the effect of the aryl group is transmitted to the carboxyl mainly by an inductive mechanism.

Correlation analysis of the half-wave reduction potentials of compounds $R.C_6H_4.X.CO.C_6H_5$ (where X represents vinylene, cyclopropylene, or a single bond) in acid medium (pH 2.4 in 50% dimethylformamide) revealed that the best results are obtained by using the Hammett σ-constants and the Taft σ^0-constants. Values of ρ (in mV) corresponding to the above bridges X were −130 (σ), −272 (σ and σ^0), and −339 (σ).[225] Since benzophenones (standard series) and cyclopropyl ketones had different mechanisms of reduction, however, the transmission factor π' unfortunately could not be calculated. The observed correlation of half-wave potentials with the σ^0-constants indicates the important part played by inductive effects in the series of cyclopropyl ketones studied.

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Effect of Conditions of Synthesis on the Structure of Polyphenylsilsesquioxane Macromolecules

I.I.Tverdokhlebova and T.A.Larina

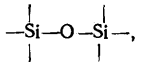
All data published up to 1973 on the hydrodynamic properties and molecular-weight parameters of organosilicon ladder polymers are surveyed. The reasons for the formation of polyphenylsilsesquioxane macromolecules of various structures are assessed. A list of 63 references is included.

Several investigations during recent years have shown that the polymerisation of compounds whose functionality exceeds two produces not three-dimensional cross-linked polymers but polymers having a two-strand linear structure[1-10]. Such systems have been termed *ladder polymers*.

The possibility of a ladder structure for several polymers was predicted by Berlin[11]. Carbon-chain ladder polymers can be obtained by the cyclisation of linear polymers, as well as by the polymerisation of polyfunctional monomers[12-14]. Among known ladder polymers are cyclopentadiene[15,16] and cyclobutadiene[17]. Aromatic ladder polymers can be obtained by the photopolymerisation of acetylenes[18]. The synthesis of ladder polyquinoxalines has been reported[19]. Ladder polymers are known comprising oxygen- and nitrogen-containing heterocycles[20,21], as well as inorganic ladder compounds[22-24]. This is by no means a complete list of work on ladder polymers belonging to various classes of compounds. Broad surveys of this topic have appeared[25,26].

Ladder polymers are of considerable interest in connection with their valuable properties due to their structural peculiarities, notably the two-strand structure of the macromolecules. Such polymers possess solubility, enhanced thermal stability, strength, and inertness towards corrosive media.

Organosilicon polymers, polyphenylsilsesquioxanes, also form ladder polymers[27-30]. Silsesquioxanes are compounds in which every silicon atom is attached to three oxygen atoms and an organic substituent: $[RSiO_{1.5}]_n$. The polycondensation of trifunctional compounds in which the functional groups are equally reactive should produce a disordered, random network[31]. However, because the functional groups differ in reactivity or the latter may vary during the reaction, and also owing to steric factors, ordered structures may be formed. The tendency of the monomer to form rings may also produce a certain ordering. Siloxanes possess the unique ability of varying the bond angle



so that the chain is very flexible, and rings varying in structure and size may be formed. The disordered, irregular structures appearing in the early stages of the reaction are able to rearrange into regular structures only when condensation occurs in the presence of a catalyst which will rupture

bonds. In the hydrolysis and subsequent condensation of phenyltrichlorosilane and other organotrichlorosilanes in the presence of alkali, for example, cagelike silsesquioxanes were isolated, as well as polymers to which a two-strand ladder structure was ascribed[28-30,32]. The main factor governing the formation of silsesquioxanes having a particular structure is the nature of the substituent attached to the silicon atom, as well as the conditions of synthesis.

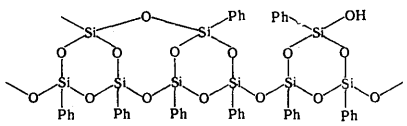


Figure 1. Structure of polyphenylsiloxane macromolecules suggested by Andrianov[2].

The first publication in which condensation of the hydrolysis products of phenyltrichlorosilane was assumed to involve the formation of internal rings, was due to Andrianov[2]. In his suggested structure (Fig. 1) every silicon atom is attached to three oxygen atoms and an organic substituent. Every unit corresponds to the formula $RSiO_{1.5}$.

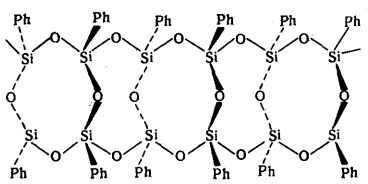


Figure 2. Structure of polyphenylsiloxane macromolecules suggested by Brown[6].

A polymer of general formula $(RSiO_{1.5})_x$ was first obtained by Brown[6] by the equilibrium condensation of hydrolysis products of phenyltrichlorosilane, and was assigned the structure shown in Fig. 2. Brown established that the main conditions governing the formation of a cyclolinear polymer during anionic polymerisation are temperature and solute concentration. Condensation of

the hydrolysis products in dilute solution (up to 5%) yields mainly oligomers of low molecular weight having a cagelike structure[28,29]. Those illustrated in Fig. 3 were isolated as pure crystals[30]. However, the cagelike compounds may also have an incompletely cyclised, defect structure (Fig. 3*b*). In the concentration range 5–7% polymers of low molecular weight (prepolymers) are formed at equilibrium. When equilibrium is established in concentrated (85–95%) solutions at 250°C, a soluble cyclolinear (ladder) polymer of molecular weight exceeding 4×10^6 is formed, to which Brown assigns a *cis*-syndiotactic structure[30]. At 100% concentration a gel is formed. With variation in solution concentration ladder polymers pass into cagelike polymers and conversely (Fig. 4).

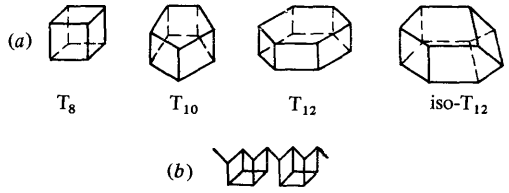


Figure 3. Cagelike compounds[28,29].

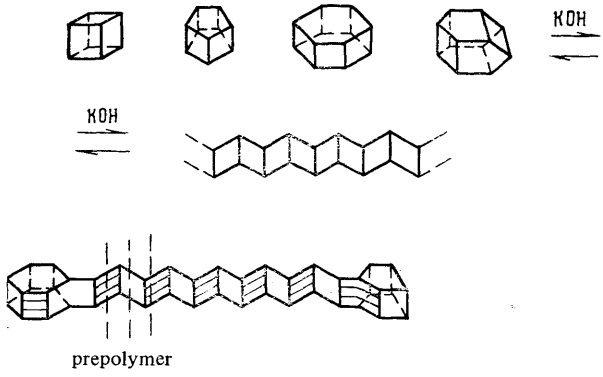


Figure 4. Conversion of cagelike compounds into a ladder polymer (and conversely).

Such ability to pass from cagelike compounds into ladder polymers was responsible for their technical application[31,33,34]. Raising the temperature of the solution converts a lower polyphenylsiloxane coating into a polymer of high molecular weight. The work of Andrianov and his colleagues supports Brown's hypothesis that cagelike compounds may pass into a ladder polymer[35,36] (Fig. 5).

The preparation of a polyphenylsiloxane of high molecular weight by condensing the hydrolysis products of phenyltrichlorosilane in the presence of caustic potash at 250°C was described[27], and the influence of the medium on the mechanical properties, molecular weight, and structure of the polymer macromolecules was studied. The higher the boiling point of the solvent, the larger the molecular weight attained by the polymer. The nature of the solvent had no significant effect on the structure of the polymer macromolecules. A mechanism of formation of a cyclolinear polymer by internal cyclisation at hydroxy-groups was suggested[37].

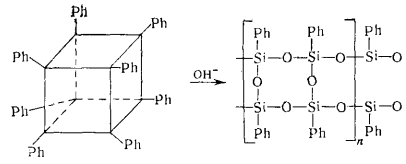


Figure 5. Transition of cagelike compounds into a ladder polymer[35,36].

Brown's conclusion that polyphenylsiloxanes obtained from hydrolysis products of phenyltrichlorosilane had a *cis*-syndiotactic structure was based on a study of the properties of solutions, X-ray examination, infrared and ultraviolet spectra, and calculation of bond angles[30]. The infrared spectra of a cyclolinear polyphenylsiloxane give a well resolved doublet in the region of 1045 and 1155 cm^{-1}. Ultraviolet spectra agree well with the suggested cyclolinear structure[29], and X-ray structural analysis shows that a chain segment comprises four units[7,30]. However, only strictly determined conditions of synthesis can yield a regular polyphenylsiloxane with a two-strand ladder structure.

The use of Stuart–Briegleb models to examine the possible formation of cyclolinear polyphenylsiloxanes suggested[32] that a regular structure could result only from the reaction of rings whose silicon atoms lay in the same plane, with either *cis*- or *trans*-hydroxyls. Analysis showed that only a *cis*-structure in the boat form, when the 1,2-hydroxyls of one monomer condense with the 3,4-hydroxyls of another monomer, can lead to the formation of a *cis*-isotactic polyphenylsiloxane having a double-chain structure. The silicon atoms then lie in one plane, with bridging oxygen atoms on one side, and chain oxygen atoms on the other side of the plane (Fig. 6).

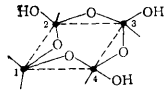
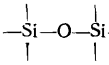


Figure 6. *cis*-Structure of T_4 in the chair form[32].

With bulky substituents (e.g. phenyl), however, the



angles are distorted. It has therefore been assumed[32] that an isotactic structure with phenyl substituents attached to the silicon atom will be formed if it is postulated that the chain can be screwed along its axis.

The hypothetical condensation of *trans*-T_4† in the chair form by condensation of the 1,2-hydroxyls of one ring with the 4,3-hydroxyls of another ring should produce a *cis*-syndiotactic ladder structure (Fig. 7). Condensation in other possible ways should produce non-cyclolinear structures, e.g. branched and network. Among such types of ring condensation are those of *cis*-T_4 in the chair form, of *trans*-T_4 in the chair form (1,2-hydroxyls of one ring with the 3,4-hydroxyls of another ring), and *trans*-T_4 in the boat form[32].

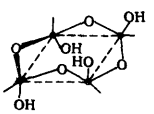


Figure 7. *trans*-Structure of T_4 in the chair form[32].

Thus all the above discussion shows that formation of a cyclolinear structure (Fig. 2) is possible but requires the observance of definite reaction conditions. In cases in which existence of *trans*-T_4 in the boat form is not energetically more favourable than other conformations, the formation of non-cyclolinear structures is possible.

The mechanism of the formation of ladder polymers is complicated and dependent on the conditions of synthesis. Formation of a double-chain structure can probably involve either condensation at free hydroxy-groups of a lower prepolymer[37] or a stage of rearrangement of cagelike compounds[38]. Frey[39] put forward the hypothesis that the resulting polyphenylsiloxane is highly ordered only in individual polycyclic segments distributed at random along the chain.

Table 1. Optical anisotropy and rigidity of various polyphenylsiloxanes (PPS).

Polymer	$10^{-5}M$	$10^{25}(\alpha_1-\alpha_2)$, cm^3	A, Å	S
PPS-1	1.0	—1230	136	54
PPS-2	0.65	—1060	84	34
PPS-3	3.7	—1800	178	71

A double-chain structure should lead to enhanced rigidity of the polymer macromolecules. This is confirmed by several studies both of the properties of polyphenylsiloxane solutions[32,37-47] and of the physicochemical properties of such polymers in the condensed state[7,38,48-52]. High chain rigidity of polyphenylsiloxane obtained by treating hydrolysis products of phenyltrichlorosilane with potassium hydroxide in various solvents was shown by an investigation of its behaviour in solution. The calculated anisotropy of polarisability of a segment $\alpha_1 - \alpha_2$ was compared with experimental values[37,40]. It was shown[53] that $\alpha_1 - \alpha_2 = +4.8 \times 10^{-25}$ cm^3 for linear polydimethylsiloxane (a single-chain polymer). The introduction of 10% of phenyl groups into the flexible polydimethylsiloxane macromolecule diminished the flexibility only slightly, although the sign changed from positive to negative: -2.4×10^{-25} cm^3. Double-chain polyphenylsiloxane was found[40] to have $\alpha_1 - \alpha_2 = -1740 \times 10^{-25}$ cm^3.

Tsvetkov et al. have shown[46] that polyphenylsiloxanes obtained by different workers possess different rigidity parameters (Table 1). According to the results of various workers[7,35,42,44,46,54] the parameter a in the Mark–Kuhn–Houwink (MKH) equation $[\eta] = KM^a$, which is connected with the flexibility of the polymer chain, varied from 0.70 to 1.50 depending on the number of fractions into which the polymer had been separated (Table 2).

Table 2. Parameters a and K in the MKH equation for polyphenylsiloxanes.

Equation	Solvent	T, °C	No. of fractions	Ref.
$[\eta] = 1.305 \cdot 10^{-7} \cdot M^{1.29}$				
$[\eta] = 1.93 \cdot 10^{-4} \cdot M^{0.63}$	benzene	20	6—10	37
$[\eta] = 1.47 \cdot 10^{-5} \cdot M^{0.916}$	benzene	25	18	
$[\eta] = 1.33 \cdot 10^{-5} \cdot M^{0.92}$	chloroform	25		
$[\eta] = 1.77 \cdot 10^{-5} \cdot M^{0.895}$	toluene	37		42
$[\eta] = 0.58 \cdot 10^{-5} \cdot M^{0.978}$	*o*-xylene	65		
$[\eta] = 1.568 \cdot 10^{-5} \cdot M^{0.897}$	θ-solvent (ethylene dichloride)	50.5		
	benzene		13	
$[\eta] = 2.38 \cdot 10^{-3} \cdot M^{0.9}$	bromoform			41
	benzene + butyl acetate (6:4)	21		
$[\eta] = 7.7 \cdot 10^{-4} \cdot M^{0.9}$	benzene		13	41
$[\eta] = 7.6 \cdot 10^{-3} \cdot M^{0.7}$	benzene			
$[\eta] = 1.3 \cdot 10^{-4} \cdot M^{1.09}$	benzene			
$[\eta] = 2.1 \cdot 10^{-5} \cdot M^{0.88}$	benzene		10	
$[\eta] = 4.898 \cdot 10^{-4} \cdot M^{0.94}$	benzene		13	44
$[\eta] = 4.624 \cdot 10^{-3} \cdot M^{0.74}$	bromoform			
$[\eta] = 1.09 \cdot 10^{-8} \cdot M^{1.48}$				
$[\eta] = 2.74 \cdot 10^{-7} \cdot M^{1.16}$	benzene	20	26	55, 56
$[\eta] = 1.25 \cdot 10^{-8} \cdot M^{1.47}$	benzene	40		
$[\eta] = 1.54 \cdot 10^{-6} \cdot M^{1.12}$	benzene	20	25	
$[\eta] = 2.66 \cdot 10^{-7} \cdot M^{1.24}$				55, 56
$[\eta] = 6.95 \cdot 10^{-7} \cdot M^{1.17}$	benzene	40		
$[\eta] = 5.41 \cdot 10^{-4} \cdot M^{0.72}$	benzene	20	25	
$[\eta] = 5.03 \cdot 10^{-4} \cdot M^{1.32}$				
$[\eta] = 8.72 \cdot 10^{-4} \cdot M^{0.68}$	benzene	25		55, 56
$[\eta] = 5.60 \cdot 10^{-8} \cdot M^{1.31}$				
$[\eta] = 5.06 \cdot 10^{-8} \cdot M^{1.32}$	benzene	40		

It must be borne in mind that, if the macromolecules possess enhanced rigidity, the intrinsic viscosity is almost independent of the solvent used for its determination and of the temperature of measurement. Its value remains almost unchanged throughout the range of molecular-weight determination in benzene, bromoform, and the θ-solvent[42,46,55]. Similar constancy of intrinsic viscosity has been observed with variation in the temperature of a polyphenylsiloxane solution. This indicated that volume (long-range) effects had no appreciable influence on the dimensions of macromolecules in solution and that the high value of the exponent a in the MKH equation was due, not to volume effects, but to the enhanced skeletal rigidity of the macromolecules[57,58].

Differences in the parameter a are therefore probably due to the presence in the polyphenylsiloxane of macromolecules not having a ladder structure. As shown above, a possible cause of the simultaneous formation of different polymer structures might be the appearance of various

† [For the "T" nomenclature cf. Ref. 29 (Ed. of Translation)].

types of polycyclic prepolymers in the initial stage of condensation[28,29,32]. Another possible reason might be increased probability of detachment of phenyl groups when reaction has proceeded for a long time, with the formation of more complicated structures, in particular strongly branched macromolecules of higher molecular weight (microgels). Guyot et al.[59] have shown that the degradation of polyphenylsiloxane consists not in depolymerisation with rupture of the two-strand siloxane bond but in the detachment of phenyl groups with the formation of benzene. This explains the improved thermal stability of the polyphenylsiloxane, since removal of a chain fragment from a ladder macromolecule—in contrast to a single-chain macromolecule—requires several simultaneous ruptures. In addition, the parameter a may vary with the proportion of defects in the macromolecules, which may be due to the presence of residual, unchanged hydroxy-groups. However, the number of such groups in polyphenylsiloxane macromolecules is so small that no method of physicochemical analysis has yet been able to accomplish their quantitative determination.

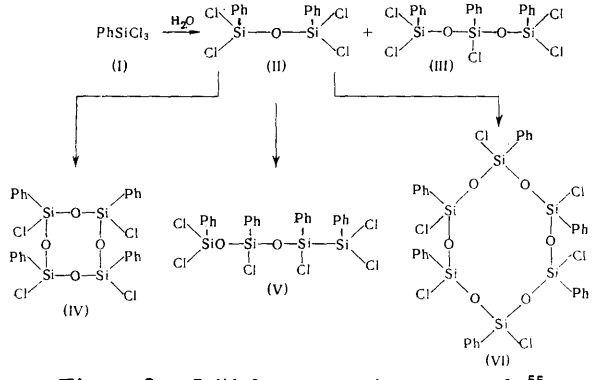


Figure 8. Initial monomeric compounds[55].

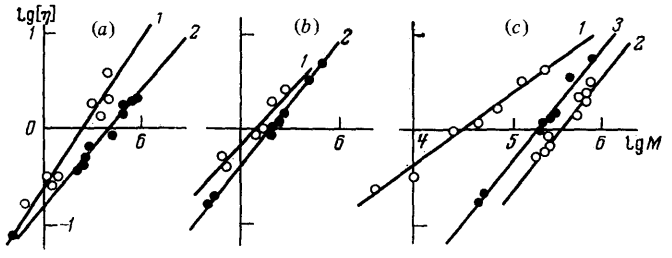


Figure 9. Dependence of $\lg[\eta]$ on $\lg M$ for polyphenylsiloxanes obtained from different monomers[55].

To examine the role of the initial monomeric compounds in forming polyphenylsiloxanes having a ladder structure, the compounds (I)–(IV) (Fig. 8)‡ were each subjected to hydrolysis under the same conditions with subsequent polycondensation and polymerisation in the presence of potassium hydroxide. All the polyphenylsiloxane fractions were found to be identical in elementary composition, which corresponded to the chain unit $(C_6H_5SiO_{1.5})_4$, but they differed considerably in hydrodynamic properties. Fig. 9 shows that the polymers consisted of two types of macromolecules differing in structure or in proportion of structural defects. All the polyphenylsiloxanes synthesised gave two straight lines when $\lg[\eta]$ was plotted against $\lg M$, with different values of the parameter a in the MKH equation: i.e. the precipitant–solvent system chosen[55] enabled for the first time the separation of polyphenylsiloxanes both according to molecular weight and according to structure (Table 2). Intrinsic viscosities obtained for the polymers $PPS(III,_3)$ and $PPS(IV,_3)$ (polyphenylsiloxanes produced by polymerising the monomers (III) and (IV) (Fig. 8) for 3 h), as well as the parameters a, were closely similar to the characteristic viscosities and the value $a = 1.29$ found[37] for polyphenylsiloxanes resulting from compound (I).

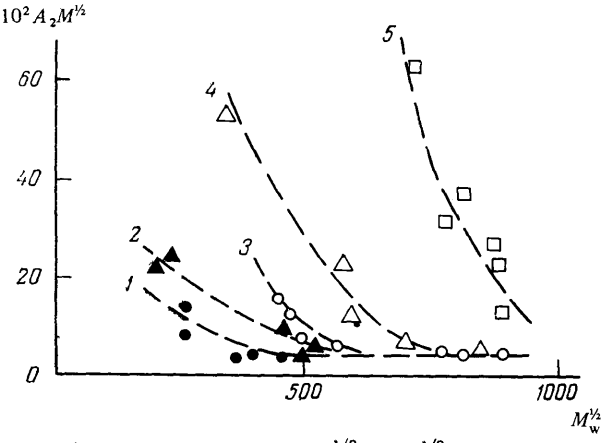


Figure 10. Dependence of $A_2M^{1/2}$ on $M^{1/2}$ for polyphenylsiloxanes with various values of a in the MKH equation: 1) 1.12; 2) 1.24; 3) 1.32; 4) 1.48; 5) 1.49.

Fig. 10 shows that polyphenylsiloxanes obtained from products of the partial hydrolysis of phenyltrichlorosilane and having different values of a in the MKH equation correspond to different variations of $A_2M^{1/2}$ with $M^{1/2}$ (where A_2 is the second virial coefficient)[56,60]. This dependence is non-linear even at quite high molecular weights, which suggests that the macromolecular chains are of finite length in this region and hence are rigid. The graph of $A_2M^{1/2}$ against $M^{1/2}$ moves to the right with increase in a. Calculations of the dimensions of the macromolecules based on several theories showed[61–63] that the rigidity parameter $[\overline{h_0^2}/M]^{1/2}$ increases with a (where $[\overline{h_0^2}]^{1/2}$ is the mean square distance between the ends of a macromolecular chain, and M is the molecular weight).

Thus a polyphenylsiloxane comprising both macromolecules having a two-strand ladder structure and a different, defective structure can be obtained depending on the nature of the initial monomer and the conditions of synthesis.

‡ [Compounds (V) and (VI) are not mentioned in the Russian text (Ed. of Translation)].

The structural defectiveness may be due to the detachment of phenyl groups when reaction continues for a long time. Cleavage of the silicon–oxygen bond under these conditions is less probable. Unchanged hydroxy-groups may also disturb the regularity of the ladder structure.

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Chromatography in a Stream of Water Vapour

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Methods of gas chromatography using water vapour as carrier gas, various ways of generating water vapour and its mixtures with other gases, and also the usefulness of various detecting systems are surveyed. The effect of water vapour on the retention and on the form of the chromatographic zones is analysed in detail. Use of a vapour eluent shows promise in preparative gas chromatography. The bibliography contains 64 references.

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I. INTRODUCTION

One of the principal directions in the development of gas chromatography is the improvement of methods for controlling the sorption properties of columns, by (i) modifying solid supports in order to eliminate the effect of adsorption on the form of the elution zones of (especially strongly polar) sorbates, (ii) modifying adsorbents to change the form (usually to straighten) the sorption isotherms of separable compounds, and also to decrease the sorption coefficients of substances having high boiling points, (iii) increasing the solubility of sorbates in the gas phase, and hence diminishing their partition coefficients between stationary and mobile phases, and (iv) using mixed stationary liquids in order to regulate the degree of separation of components of complicated mixtures.

The use of water vapour as mobile phase is an extremely effective procedure for controlling sorption characteristics in the above ways. In gas–liquid chromatography, water vapour interacts with active centres in the solid support, and may also form binary systems with stationary liquids whose composition is regulated by the use of mixed eluents. In gas-adsorption chromatography the blocking of adsorption centres by water molecules ensures more symmetrical sorbate peaks, together with substantial acceleration of the analysis. Conditions can also be chosen under which an aqueous layer, which acts as sorbent in the chromatographic process, is formed on the adsorbent (or inert support). Finally, the solubility of sorbates in the mobile vapour phase can be increased to a certain extent by raising the pressure in the column.

Use of a vapour eluent also has other advantages—(*a*) the possibility of working both with some detection systems for gas chromatography (catharometer, flame-ionisation detector, etc.) and with systems which detect in the liquid phase, (*b*) cheapness, enabling this eluent to be used in high-output preparative apparatus and works chromatographic equipment, and (*c*) the possibility of complete condensation of the eluate without the use of low temperatures, which almost completely eliminates loss of material in the traps of chromatographic equipment.

The impossibility of analysing readily hydrolysable substances, of course, imposes a significant limitation on the use of water vapour. Furthermore, the danger of condensation imposes a temperature restriction.

The advantages of water vapour as a mobile phase, resulting from the possibility of modifying the solid support, were realised in 1958 by Knight[1], who, on saturating helium as carrier gas with water vapour, observed an increase in symmetry of the chromatographic zones of alcohols, amines, and water. Similarly, in 1964 Kolesnikova et al.[2] worked with moistened helium and obtained symmetrical water peaks. It was noted in particular that moistening the helium changes the sequence of elution of water and butanol. Still earlier, in 1957, Turkel'taub et al.[3] saturated the air carrier gas with water vapour in order to study the effect of the moisture content of silica gel on the chromatographic separation of gases. Water vapour was first used directly as eluent in 1960[4] (this was a continuation of earlier work[5] in which the eluent was alcohol vapour). Photocolorimetric detection was used. At the same time (1960) a Japanese patent was issued[6] on the use of water vapour as mobile phase, and a similar method was described later[7].

In 1964 Davis et al.[8], using a mixture of helium and water vapour as mobile phase, achieved a sensitivity of $2 \times 10^{-6}\%$ of ethanediol with the use of a flame-ionisation detector. Similarly, a mixture of nitrogen and water vapour was used to analyse aqueous solutions of organic acids[9]. Lowering the column temperature with a mixture of water vapour and helium results in a layer of water forming on the solid support; this serves as stationary phase for separating both polar and non-polar substances[10-12]. Beginning in 1967 Nonaka published a series of investigations on chromatography in water vapour using a flame-ionisation detector[13-22]. Mixtures of n-alkanes, aromatic hydrocarbons, alcohols, amines, aldehydes, acids, etc. were analysed, including aqueous emulsions and suspensions of concentration $10^{-2}-10^{-4}\%$. Fig. 1 shows some of the chromatograms obtained in these researches. Similar materials were analysed by Rudenko and his coworkers[23,24].

In a later paper Nonaka [21] added formic acid and hydrazine hydrate to the water vapour in order to block adsorption centres on the solid support more completely when analysing aliphatic acids and alkylamines (by analogy with a principle suggested by Knight [1]). Zhukhovitskii and his coworkers [25-27] have shown the suitability of water vapour for determining impurities in water and in salt solutions. They developed a two-stage method involving the use of a column on which water vapour is sorbed better, and a second column in which it is sorbed worse, than the impurities to be determined. Use of a flame-ionisation detector enables a sensitivity of 5×10^{-7}% to be achieved. The present Reviewers have investigated [28] the chromatographic separation of substances under steam pressures of 1–8 atm in the column. Raising the pressure tended both to shorten the analysis and to give more symmetrical peaks of polar sorbates (Fig. 2).

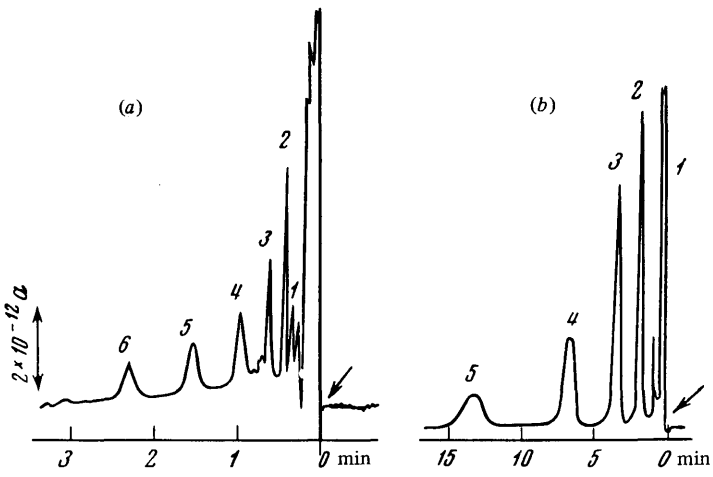

Figure 1. Chromatograms of solutions of polar compounds obtained in a flow of water vapour [20].
(*a*) Glass column of length 2.6 m and internal diameter 2.2 mm filled with firebrick (LBK-28) modified with hydrogen fluoride, with a stream flow of 71 ml min^{-1} at 130°C: 1) methanol; 2) ethanol; 3) propan-1-ol; 4) n-butanol; 5) n-pentanol; 6) hexanol.
(*b*) Glass column of length 2.6 m and internal diameter 1.8 mm filled with Chromosorb PAW with 3% of ortho-phosphoric acid and a steam flow of 42 ml min^{-1} at 170°C: 1) solvent (carbon tetrachloride); 2) lauric acid; 3) myristic acid; 4) palmitic acid; 5) stearic acid.

In 1973 Mar'yakhin and one of the present Reviewers [29], Rudenko et al. [30,31], and also Klesment [32] used water vapour as eluent in preparative gas chromatography.

Conditions for the separation of substances in a stream of water vapour or its mixtures are given in the Table.

II. PREPARATION OF MOBILE PHASE

A mixed eluent can be generated by saturating a gas with water vapour by passing the former either through a moistened granular layer [1] or over the surface of water [9]. A mixed eluent can be obtained also by bubbling through a thermostatted water layer [10]. Helium was passed [1] through a tube 0.6 m in length and 6 mm in diameter immersed in a water bath; the tube was filled with moistened C-22 support, and the relative humidity of the gas at the outlet from the column was ~50% at room temperature. A current of nitrogen entered [10] the lower part of a thermostatted steel vessel, in which it bubbled through a layer of water; the temperature of the vessel was 70 to 95 ± 0.1°C, and that of the tube connecting it with the chromatograph injector was 100°C.

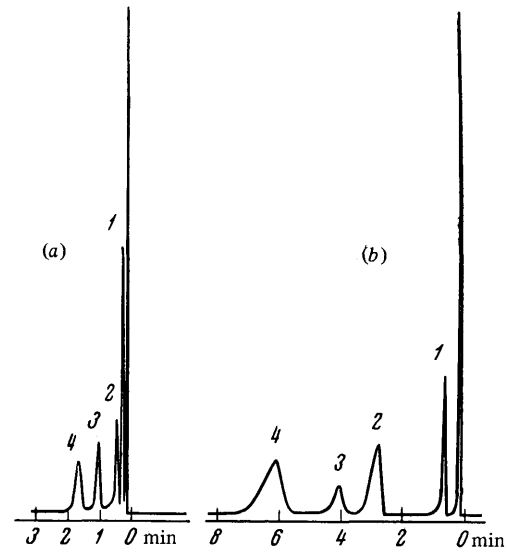

Figure 2. (*a*) Chromatogram of a mixture of normal alcohols and aniline obtained at 125°C on a column of length 0.7 m and internal diameter 2.9 mm filled with high-vacuum silicone grease applied to Chromosorb W: 1) hexanol; 2) aniline; 3) nonanol; 4) decanol.
(*b*) Chromatogram of a mixture of dialkyl phthalates obtained at 170°C on column (*a*): 1) dimethyl; 2) di-isobutyl; 3) dibutyl; 4) di-isopentyl.

Fig. 3*a* represents the system for obtaining a mixed eluent used by Mori and Arimoto [9]. The steam generator was a horizontal thermostatted cylinder half filled with water. Nitrogen passed over the water and entrained the vapour above its surface.

Fig. 3*b* illustrates equipment for generating pure water vapour [4]. Water from the reservoir *1* was transferred at 0.075–0.05 ml min^{-1} by the pump *2* through a microheater *3* comprising a stainless-steel U-tube of length 30 cm and diameter 4 mm placed in a metal cylinder. The column was covered throughout its length with asbestos string, on which was wound nichrome wire. From the microheater the vapour entered a glass chromatographic column, at the outlet from which it condensed and was guided to the detector.

Conditions of separation in a stream of water vapour or its mixtures.

Compounds	Eluent	Sorbent	Column temp., °C	Detectors*	Ref.
Alcohols, water, alkylamines	He sat. with H_2O; He sat. with (H_2O + amine)	di-isodecyl phthalate, tricresyl phosphate, triethylene glycol, $\beta\beta'$-oxydipropionitrile on firebrick; 10% polypropylene glycol on firebrick; 10–40% Silicone DS-550 on firebrick	60	ca	1
Phenol, cresols, 2,4-xylenol, thymol, carvacrol, guiacol, eugenol	steam	glycerol, cholestrol, silicon grease on brick	115, 120, 150	ph	4,33
n-Alcohols(C_{12}, C_{14}, C_{16}); *NN*-dimethylbenzylamine	steam	5% Silicone SE-30 on diatomite	200	–	34
Alcohols (C_1–C_5), water	He sat. with H_2O	30% polyethylene glycol 600 on brick	100	ca	2
Aqueous glycols	He + H_2O	hexaphenyl ether on Teflon	110, 150	fi	8
n-Alcohols (C_1–C_5), glycols, menthol (extracted with alcohol from cigarette smoke)	N_2 + H_2O	H_2O on Gas Chrome CLZ and on silanised Chromosorb W	70–94	fi	10
n-Alkanes, formates, aldehydes, amines, alcohols (study of thermodynamics of dissolution in water)	He sat. with H_2O	H_2O on Chromosorb	20, 30, 40	fi	54
Aqueous (0.01%) alcohols, aldehydes, ketones, esters	steam	HF-modified firebrick; Isolite (50% SiO_2)	110–210	fi	13
Polyalcohols, organic acids, phenols, amines	steam	KF- or H_3PO_4-modified brick; Chromosorb P with 3% H_3PO_4; MgO	100–270	fi	14
Aliphatic acids (C_2–C_{18}); dil. aq. benzoic, salicylic, lactic acids	steam	Chromosorb P with 3% H_3PO_4	135–230	fi	15
Phenol, cresols, 2,4-dimethylphenol, *p*-ethylphenol, *p*-t-butylphenol (dil. aq. solns.)	steam	Chromosorb PAW with 3% H_3PO_4	135–205	fi	16,20
Pentane solns. of C_{10}–C_{14} *n*-alkanes	He sat. with H_2O at 20°C	46% H_2O on Chromosorb P	20	fi	11
n-Alkanes (C_{10}–C_{18}, C_{24}), octane isomers	He sat. with H_2O at column temp.	4–46% H_2O on Chromosorb P; 10% H_2O on Porasil C treated with HNO_3 + H_2SO_4 and washed to neutrality	20–85	fi	12
n-Alkanes (C_1–C_6), benzene, toluene ($\geqslant 5 \times 10^{-7}$% in H_2O and salt solns.)	steam	hydrophobic silica gel; activated carbon BAU; Apiezon L on Celite 545	110–180 (programmed)	fi	25,26, 27
Aqueous (0.5–0.02%) acids—aliphatic C_6–C_{18} and dicarboxylic, iso- and tere-phthalic, citric	N_2 + H_2O	diatomitic solid support (Shimalite AW) treated with 1.5% H_3PO_4	230–290	fi	9
n-Alkanes (C_5–C_9), benzene, toluene, isomeric xylenes, ligroin (as 0.1–10^{-4}% aq. emulsion)	steam	alumina	110–260	fi	17,19, 20
Naphthalene, 1- and 2-methylnaphthalenes, anthracene, chrysene, terphenyl, triphenylene, biphenyl, quaterphenyl (as 0.01–10^{-4}% aq. emulsion or suspension)	steam	Chromosorb PAW	130–260	fi	18,20
N-Alcohols (C_1–C_6), aldehydes, ketones, ethers, alkylamines, pyridine, aniline, toluidine, glycols, C_2–C_{18} aliphatic acids and esters, dicarboxylic acids	steam	diatomitic brick modified with HF, KF, or KHF_2; diatomitic brick ignited after addition of H_3PO_4; ignited MgO	110–260	fi	20
Aliphatic acids (C_2–C_{18}), alkylamines (C_3–C_{18}), ethylenediamine, aminoethanol	steam + 10% formic acid; steam + 20% hydrazine hydrate	Corning GLC-100 porous glass beads, Chromosorb GAW	125–200	fi	21
n-Alcohols (C_6–C_{10}), di-isoalkylamines, aniline, benzylamine, dimethylaniline, ethylaniline, diethylaniline, aliphatic acids (C_2–C_6) (including 0.05% aq. solns.)	steam	10% polyethylene glycol 4000 on Chromaton; 10% polydimethylsiloxane SKTV-1 on Chromaton	150	fi	24
n-Alkanes (C_{10}–C_{15}), di-isoalkylamines, benzylamine, mono- and di-methyl- and -ethyl-benzylamines (preparative isolation)	steam	SKTV-1 polydimethylsiloxane on Chromaton; polyethylene glycol adipate on Chromosorb A	130–210	fi	30,31
Alkanes, alkylbenzenes (preparative isolation)	steam; N_2 + H_2O	25% polyethylene glycol adipate on Spherochrome-1	120–140	fi	29
Coal tars (preparative separation)	steam	21% Apiezon L on Rysorb C (flow from fractionating column)	programmed at 20–55 deg h^{-1}		32

*Detectors: ca = catharometer; ph = photocolorimeter; fi = flame-ionisation detector.

In the apparatus used by Nonaka [13–21] (Fig. 3*c*) one stage in the preparation of the eluent was purification of the stream over copper oxide at 500–600°C.

The Reviewers used the arrangement in Fig. 3*d* to examine the chromatographic behaviour of substances under high pressures of water vapour. Nitrogen from a cylinder entered the upper part of a vessel half filled with distilled water. From here the nitrogen pressure transferred water to a tube located in the thermostat and filled with metal turnings to increase the evaporating surface. The resulting water vapour passed through a buffer vessel to diminish fluctuations in the flow rate, and entered the chromatographic column, in which the required pressure was established by means of a capillary at the outlet. Most of the water vapour then escaped into the atmosphere, and only a small quantity entered the flame-ionisation detector. The flow of water vapour through the column could be regulated by varying the pressure of the nitrogen entering the vessel *7*.

In 1962 standard equipment was advertised for generating steam for use in gas chromatography [34]. The device comprised a steel boiler containing an electric heater and fitted with a safety valve. Steam production reached 1 litre min^{-1} at pressures up to 3 kg cm^{-2}. Mixtures of water vapour with nitrogen of controllable composition could also be obtained.

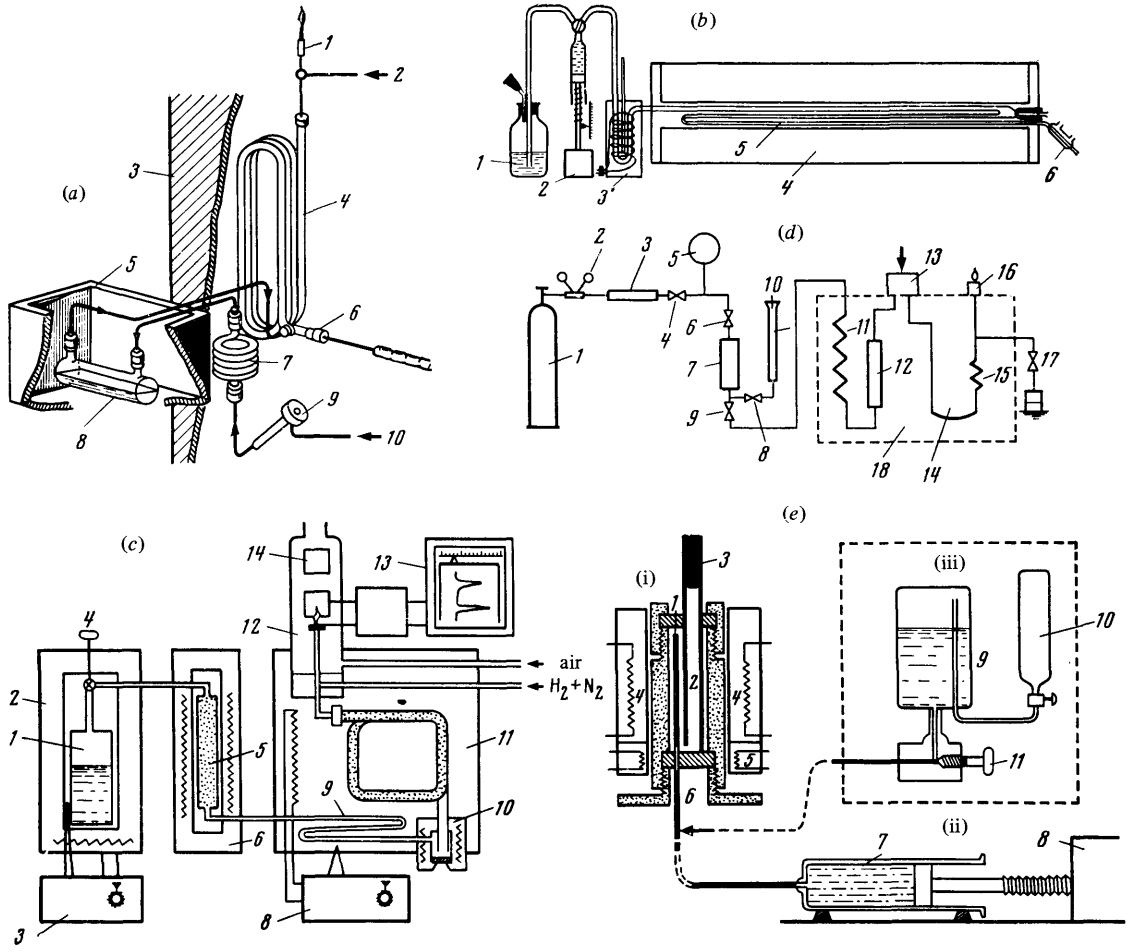

Figure 3. Diagrams of types of chromatographic apparatus. (*a*) Apparatus for operations with mixed eluent [9]: 1) flame-ionisation detector; 2) hydrogen; 3) thermostat for columns; 4) glass column; 5) thermostat for steam generator; 6) sample introduction; 7) helical tube; 8) steam generator; 9) unit for admission of carrier gas; 10) carrier gas. (*b*) Apparatus for chromatography in a flow of water vapour [4]; 1) water reservoir; 2) pump; 3) steam microgenerator; 4) thermostat; 5) glass column; 6) condenser. (*c*) [Alternative] apparatus for chromatography in flow of water vapour [13-20]: 1) steam generator; 2) electrical heater for generator; 3) thermoregulator for generator; 4) needle valve; 5) column containing CuO; 6) CuO column heater; 7) air thermostat; 8) thermostat controller; 9) buffer for water vapour; 10) introduction of sample; 11) analytical column; 12) flame-ionisation detector; 13) recording system; 14) hygrometer. (*d*) Apparatus used by Reviewers: 1) nitrogen cylinder; 2) high-pressure regulator; 3, 4, 6, 8, 9, 17) needle valves; 5) standard manometer; 7) vessel containing distilled water; 10) funnel for filling (7); 11) preliminary column filled with metal turnings; 12) buffer vessel; 13) introduction of sample; 14) chromatographic column; 15) capillary; 16) flame-ionisation detector; 18) thermostat. (*e*) Apparatus for generating mixtures of water vapour with formic acid and with hydrazine hydrate [21]: i) evaporator; ii) liquid pump; iii) alternative solution feed system; 1) eluent evaporator; 2) point of introduction of sample; 3) analytical column; 4) electrical heaters; 5) electrical heater for membrane; 6) capillary for feeding eluent; 7) glass syringe; 8) driving mechanism; 9) vessel containing water or solution; 10) gas cylinder; 11) needle valve.

Nonaka [21] used a modified chromatograph evaporator (Fig. 3*e*) to evaporate mixtures of water with formic acid and hydrazine hydrate. The Reviewers varied the pH of water vapour by placing aqueous formic acid and ammonia of various concentrations in vessel 7 in Fig. 3*d*.

The flow of the vapour eluent in the column was not measured directly in several investigations, owing to the difficulties encountered. Nonaka [20] used a specially designed hygrometer to determine the flow of water vapour. The weight of water G (in g min^{-1}) condensed at the outlet from the column has been measured [29], and hence the flow of vapour calculated by means of the equation

$$V_a = \frac{G \cdot P \cdot v}{P_0} \qquad (1)$$

where v is the specific volume of the vapour at pressure P in the column and the temperature of the column, and P_0 is the atmospheric pressure.

The Reviewers made preliminary use of an ordinary carrier gas to measure

$$C = \frac{V_\alpha j t_{0i}}{g} \quad (2)$$

where V_α is the speed of the gas leaving the column at the temperature of the latter, t_{0i} the retention time of the unsorbed substance, g (g) the weight of the stationary liquid or the adsorbent, and j the pressure gradient factor. The specific retention volume with the vapour eluent was then calculated by means of the formula

$$V_g^T = \left(\frac{t_R}{t_0} - 1\right) \cdot C \quad (3)$$

where the retention times of sorbate and unsorbed substance t_R and t_0 were measured in a stream of water vapour. In both cases methane was used as unsorbed substance.

III. DETECTION

Several of the usual chromatographic detectors are entirely suitable for working with water vapour. Knight [1] used a catharometer to detect substances in a flow of helium saturated with water. Comparison of the thermal conductivity of water vapour with those of other substances indicates that a catharometer can be used with chromatography in water vapour provided that the flow is sufficiently accurately stabilised to avoid fluctuations. Apparently a density balance can also be used in work with water vapour. The temperature of the detectors should, of course, be such as to exclude the possibility of condensation of the vapour.

An argon detector is obviously unsuitable for work with water vapour [35,36]. It was shown [37] that a tenfold increase in the concentration of water in argon (from 10^{-5} to 10^{-4} vol.%) diminishes the sensitivity of the detector by 75%. The permissible concentration of moisture in the gas for a helium detector is 10^{-4}%. [38] The range of linearity of the detector readings becomes shorter with increase in the concentration of water.

A flame-ionisation detector is most suitable with chromatography in water vapour, since it is only slightly sensitive to water. This detector has almost invariably been used with this eluent. Although the signal of a flame-ionisation detector for water is very small, it is considered to exist [39]. Water present in a sample influences the sensitivity of a flame-ionisation detector to substances eluted with it [40]. However, Amirov et al. have found [41] that the sensitivity of such a detector to water is 0.01–0.001% of its sensitivity to benzene, a conclusion confirmed by another worker [42]. The background current of a flame-ionisation detector doubles with increase in the concentration of water in argon from 10^{-4} to 1%. [43] Nevertheless, increasing the concentration of water in argon by a factor of 10^4 (from 10^{-6} to 10^{-2} vol.%) diminishes the sensitivity of the detector to ether by only 29%. When the oxygen supplied to the detector burner was saturated with water at various temperatures [44], saturation up to 12.2 mole % lowered the sensitivity of the detector by 18.7%. Water can be determined by using carbon monoxide instead of hydrogen in the flame-ionisation detector, whose sensitivity is improved by adding small quantities of water or hydrogen to the carbon monoxide. Thus the above results justify the use of a flame-ionisation detector in chromatography using water vapour as eluent. The decrease in sensitivity in the presence of water vapour is so small that very dilute ($5-10 \times 10^{-7}$%) solutions of organic substances can be analysed [20,26]. Nonaka [20] used additional preheating of the detector to avoid condensation of water vapour in the burner. A flame-ionisation detector made of glass [46] has been used [24]. Furthermore, detectors based on automatic titration of the eluate may be suitable for work with a vapour eluent [47].

IV. EFFECT OF WATER VAPOUR ON THE RETENTION AND ON THE ZONE PROFILES OF THE CHROMATOGRAPHED COMPOUNDS

No exhaustive theory has been published to describe the effect of water vapour on the retention and the spreading of chromatographic zones. However, existing results show that water vapour can successfully be used as mobile phase both in gas-adsorption and in gas–liquid chromatography. In the former the water blocks certain active centres of the adsorbent, tending to straighten the sorption isotherms of the test substances. If the stationary liquid in gas–liquid chromatography does not dissolve water, the effect of water vapour is to modify the solid support. In these cases competitive adsorption occurs between water vapour and the test sorbates, the former usually being the more strongly adsorbed, so that elution is accompanied by a displacement effect. Fig. 4 shows as example chromatograms obtained [34] for a mixture of alcohols, with water vapour and nitrogen as eluent. This phenomenon is not observed, of course, if the support or the adsorbent is hydrophobic. The dissolution of water in the stationary liquid produces a binary stationary phase, whose ability to sorb the test substances can be controlled by varying the water content (by varying the temperature, the water vapour content of the mixed eluent, or the pressure).

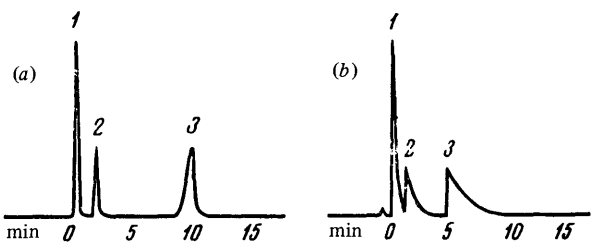

Figure 4. Chromatograms obtained [34] on column containing 5% Silicone SE-30 on diatomite at 200°C with different carrier gases (pressure at inlet 1.4 kg cm^{-2}): *a*) stream; *b*) nitrogen for n-alcohols: 1) dodecyl; 2) tetradecyl; 3) hexadecyl.

Measurements have been made in the Reviewers' laboratory [29] of the linear retention index of aromatic hydrocarbons on a column containing 25% of polyethylene glycol adipate on Spherochrome-1 with nitrogen and steam eluents at various temperatures. The change to water vapour produced a significant increase in the retention indices, especially at lower temperatures: at 130°C the indices of the aromatic hydrocarbons in water vapour exceed those in nitrogen by 1–1.5, which corresponds to 100–150 on Kováts logarithmic scale. This increase is due to the shortened retention times of the n-alkanes used as standards. A similar increase

in the logarithmic retention indices of polar compounds has been observed [24] in water vapour at 150°C, the shift amounting to 50–80 for organic acids. The composition dependence of linear retention indices for a mixed eluent (nitrogen plus water vapour) was almost linear [29].

The replacement of nitrogen by water vapour and dissolution of the latter in the stationary phase leads to a change in form of the sorption isotherms [29]. Whereas with nitrogen the peaks for aromatic hydrocarbons were usually blurred mainly at the tail (provided that samples were sufficiently large), predominant spreading of the front was observed in water vapour. The peaks of n-alkanes, characterised by spreading of the front, became still more unsymmetrical on passing to water vapour. Thus the form of the chromatographic peaks can be controlled by varying the composition of the eluent. With small samples the efficiency of a column operating with steam is quite high. According to Nonaka [20] the height equivalent to a theoretical plate may be 1–2 mm, the optimum speeds of the mobile phase being almost the same as with the usual eluents.

When the column is filled with a solid support at a temperature below the dew-point, a layer of water is formed on the support, and serves as mobile "stationary" phase for separating mixtures. Volatile solvents were first used as "stationary" phases in 1958. [48] Porter and Johnson [49] studied the behaviour of volatile solvents as mobile and liquid phases under conditions of circulatory chromatography. In a detailed study of the behaviour of mobile organic liquid phases in gas chromatography [50,51] heptane, benzene, ethanol, and other compounds served as both gas and liquid phases. These compounds have recently been used as mobile phases [52,53]. Water has served simultaneously as vapour and liquid phases [10-12,54]. Phifer and Plummer [10] analysed polar compounds with good solubility in water, which ensured considerable retention of them in the column.

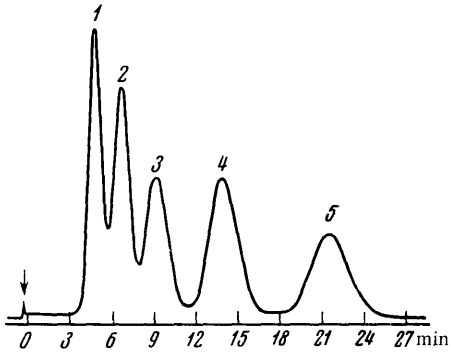

Figure 5. Separation of C_1–C_5 n-alcohols in a flow of a mixture of nitrogen and water vapour [10] at 70°C: 1) pentanol; 2) butanol; 3) propanol; 4) ethanol; 5) methanol:

It is interesting that, since water interacts by means of hydrogen bonds with alcohols undergoing analysis, the elution sequence observed is opposite to the usual order (Fig. 5). Karger et al. [11,12] investigated the behaviour of non-polar sorbates, which, being almost insoluble in water, were eluted very rapidly from the column. The relative rate of elution of alkanes on a column with water exceeded those on columns with Apiezon and with polyethylene glycol by factors of 30 000 and 67 respectively. On a column with water n-tetracosane is eluted even at 85°C, which is 306 deg below its boiling point (the vapour pressure of n-tetracosane at 85°C is 2×10^{-4} mmHg). In the separation of n-alkanes the ratio of the degree of separation to the duration of analysis on a column with water at 20°C exceeded that on a column with squalane by a factor of 12. This confirms the conclusion [55,56] that the rapidity of analysis of non-polar compounds is increased on passing to polar stationary phases. Karger et al. showed that the activity coefficients of n-alkanes in water are of the order of 10^6. According to Pecsap and Martin [54] these quantities for C_5–C_7 n-alkanes are $(1-8) \times 10^3$ at 20°C. These workers studied also the thermodynamics of the dissolution in water of various other organic compounds, including alcohols, aldehydes, and chlorinated methanes.

Water was used as stationary liquid in earlier work [57,58] to separate chlorinated methanes at 20°C. Here, however, a dry carrier gas was used initially. Varying the percentage impregnation of kieselguhr with water led to a change in the elution sequence of the sorbates.

Giddings et al. [59,60] studied the effect of surface-active additives on the efficiency of a column with water deposited on glass beads. The carrier gas was moistened helium. Experiments at 2°C showed that a small addition to water of a surface-active agent, in particular hexadecanol, led to marked broadening of the sorbate peak owing to the additional resistance to mass transfer at the surface.

V. PREPARATIVE GAS CHROMATOGRAPHY

The use of water vapour and its mixtures in preparative gas chromatography is extremely promising, since it will lower the economic cost, enable the selectivity of the column to be controlled, and also ensure complete recovery of the separated substances. In particular, water vapour and its mixtures with organic vapours will ensure complete condensation of the eluate after passing through the column even at ordinary temperatures by the use of running water as coolant [29]. Such a procedure enables losses of separable substances to be almost eliminated, and of course is preferable to published methods [61-63] of the low-temperature condensation of argon and carbon dioxide emerging from the column.

It is interesting that, if the eluent is a mixture of water vapour and the vapour of a water-insoluble organic compound, condensation of the eluent in the trap is followed by extraction of the separable substance, which condenses in one of the phases (aqueous or organic). Thus the proportions of the components of the mobile phase (water vapour and organic eluent) should be chosen, depending on the nature of the separable substances, to ensure that the latter is concentrated sufficiently.

Preparative isolation of individual aromatic hydrocarbons has been accomplished [29] on a column of internal diameter 20 mm and length 3.2 m containing 25% of polyethylene glycol adipate on Spherochrome with water vapour and its mixtures as carrier gas. Hydrocarbons and polar compounds have been isolated [30,31] in a flow of water vapour on columns of a silicone and of polyethylene glycol acetate. It has also been reported that water vapour may be used in projected industrial chromatographic equipment, which would eliminate the eluent recirculation and fine purification system [64].

An original method for the preparative separation of complicated mixtures by combining fractional distillation with chromatography in a stream of water vapour has been suggested by Klesment [32]. The separable mixture (coal or shale tar) was run into the still of a fractionating column and steam-distilled, with the flow from the upper part of the column (of height 40 cm and efficiency 7–10 theoretical plates) continuously entering a chromatographic column of length 2.8 m and internal diameter 12 mm containing 21% of Apiezon L on Rysorb C operating with temperature programming. Narrow fractions (0.2–1 ml) were collected in vacuum receivers (residual pressure 50 mmHg) at equal time intervals. Fractions boiling up to 400°C were isolated by the above method.

Thus the use of water vapour as mobile phase represents a definite stage in the development of gas chromatography.

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Compatibility of the Methods of Calculation and Semiempirical Parameters in the Theory of Molecules with Conjugated Bonds

I.A.Misurkin and A.A.Ovchinnikov

Various methods for the selection of the parameters of the model π-electron Hamiltonian are discussed, certain aspects of the interaction of π electrons with the σ skeleton are considered, and the scope of various methods for the calculation of the electronic structures of molecules and radicals wtih conjugated bonds are analysed.
The bibliography includes 90 references.

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1. INTRODUCTION

The modern theory of the electronic structures of compounds with conjugated bonds employs the π-electron approximation, which has been analysed in detail in a previous review by the present authors[1]. According to this approximation, it is possible to obtain all the observed characteristics of conjugated many-electron systems if only the π electrons are considered explicity in the quantum-chemical calculation. The properties of π electrons are specified by an effective model Hamiltonian[4]:

$$H = \sum_{p,q,\eta} h_{pq} c^{+}_{p\eta} c_{q\eta} + \sum_{p,q,\eta,\rho} \gamma_{pq} c^{+}_{p\eta} c_{p\eta} c^{+}_{q\rho} c_{q\rho}, \qquad (1)$$

where $c^{+}_{p\eta}$ and $c_{p\eta}$ are the operators of the creation and annihilation of an electron with a spin η in the state with the function $\varphi_p(\mathbf{r})$ localised at an atom p, h_{pq} is the one-electron parameter for the kinetic energy and the energy of attraction of the σ skeleton, and γ_{pq} is the parameter for the Coulomb repulsion of the π-electrons at the atoms p and q.

A minimal representation of second quantisation is employed in the review: in formulating the Hamiltonian and other operators and in considering the derivation of important results obtained by Linderberg (in Section 2, a).

In the present review attention is concentrated on the problem of the consistency between the method of calculation and the calculated molecular characteristics and also the problem of consistency between the semiempirical parameters (h_{pq}, γ_{pq}, etc.) and the method of calculation. Certain problems of the interaction of π-electrons with the σ skeleton, where the question of the π-electron approximation and its possibilities becomes most acute, are likewise examined.

2. VARIOUS METHODS FOR THE DETERMINATION OF THE PARAMETERS OF THE MODEL π-ELECTRON HAMILTONIAN

We shall consider certain methods or schemes for the parametrisation of the effective model Hamiltonian which differ from the two general parametrisation schemes (Scheme 1 and Scheme 2) examined in the previous review[1]. All these schemes normally give good agreement with experiment and similar effective Hamiltonian parameters. Such are the parametrisation schemes for conjugated systems with N and O heteroatoms[2] and with amino-groups[3], and for conjugated hydrocarbons[4]. In these studies the authors altered somewhat the generally accepted values of the parameters in order to achieve a better description of the experimental data for molecules of the specified type. Calculations have been made[5] on heterocyclic conjugated molecules with N, O, and S atoms and in a subsequent study[6] fairly combersome formulae were proposed whereby all the empirical parameters of the earlier investigation[5] were reproduced with satisfactory accuracy (using Slater's $2p_z$ functions). These formulae were obtained from model physical ideas concerning the π-electron system and the σ skeleton.

This parametrisation procedure is convenient in computer calculations and is formally (but not in reality) less empirical than Scheme 1. Empirical information is contained, as in Scheme 2, in the effective charges of Slater's functions and in the special form of the formulae for the parameters[1,6].

The simple parametrisation schemes of the Pariser–Parr–Pople (PPP) method (neglect of the parameters of the Coulomb interaction between electrons in non-adjacent atoms, neglect of the relation between $\beta_{\mu\nu}$ and $R_{\mu\nu}$, etc.) have been used in calculations on polysubstituted benzenes and five-membered heterocycles with N, O, and S atoms[7], azabenzenes and azanaphthalenes[8], and substituted benzenes, pyridines, and pyrimidinones[9]. It is interesting to note that the optimal values of the same parameters of the model Hamiltonian for molecules of different homologous series differ somewhat as a rule. This is typical for a semiempirical theory.

In one of the parametrisation schemes for hydrocarbons[10,11] the benzene excitation energies (as in the old Pariser–Parr method[12]) and the benzene ionisation potential are used to determine $\gamma_{\mu\nu}$ and βCC. If the excitation energies (in terms of the ZDO approximation) depend on the differences between the $\gamma_{\mu\nu}$, then the $\gamma_{\mu\nu}$ themselves enter into the expression for the ionisation potential obtained using Koopman's theorem. As a result, somewhat unusual values of the parameters were obtained for benzene: βCC = −2.4 eV and γ_{11} = 9.4 eV[10] or βCC = −2.5 eV and γ_{11} = 8.2 eV.[11] The remaining $\gamma_{\mu\nu}$ were estimated from formulae of the Mataga–Nishimoto type[12].

We believe that it is more natural to employ a corrected Koopman's relation [see the previous review[1], formula (32)] or to compensate the inaccuracies in the Koopman's relation by introducing a special parameter ΔW_0 [see the previous review[1], Eqns. (15)–(17)], as was done in Scheme 1, particularly since the improvements introduced by the new parameters are insignificant. For example the energy of the $S \rightarrow T$ transition in anthracene is ΔE = 1.84 eV (experimental value), ΔE = 1.79 eV (value obtained with the new parameters[10]), and ΔE = 1.66 eV (value calculated by the PPP scheme taking into account excited configurations made up from Hückel molecular orbitals[13]).

a. The Linderberg Method for the Calculation of Resonance Integrals

The new possibilities for the creation of a unified parametrisation scheme for the effective Hamiltonian arose after the publication of Linderberg's study[14]. In order to calculate the resonance integral $\beta_{\mu\nu}$ or the parameter $h_{\mu\nu}$ in the PPP(1) Hamiltonian, Linderberg employed a familiar quantum-mechanical relation for the momentum $\mathbf{p}$ in terms of the commutation relation

$$[\mathbf{r}, H] \equiv \mathbf{r}H - H\mathbf{r},$$

the coordinates $\mathbf{r}$, and the Hamiltonian H:

$$i\hbar \frac{d\mathbf{r}}{dt} = [\mathbf{r}, H] = i\hbar \frac{\mathbf{p}}{m}, \qquad (2)$$

where H is the PPP(1) Hamiltonian, $\hbar$ the Planck constant, and m the mass of the electron. In the second quantisation representation the operators $\mathbf{r}$ and $\mathbf{p}$ can be expressed as follows in terms of the electron creation and annihilation operators:

$$\mathbf{r} = \sum_{q,\eta} \mathbf{R}_q c^+_{q\eta} c_{q\eta}, \qquad \mathbf{p} = \sum_{\nu \neq s, \eta} \mathbf{p}_{\nu s} c^+_{\nu\eta} c_{s\eta}, \qquad (3)$$

where $\mathbf{R}_q$ is the coordinate of the atom q with which the basis function $\varphi_q(\mathbf{r})$ is associated. The matrix element $\mathbf{p}_{\nu s}$ has the following form (ν and s are neighbouring atoms):

$$\mathbf{p}_{\nu s} = \int \varphi_\nu(\mathbf{r})(-i\hbar\nabla)\varphi_s(\mathbf{r})\,d\mathbf{r} = \int \varphi(\mathbf{r}-\mathbf{R})(-i\hbar\nabla)\varphi(\mathbf{r})\,d\mathbf{r} = -i\hbar\nabla_R \int \varphi(\mathbf{r}-\mathbf{R})\varphi(\mathbf{r})\,d\mathbf{r} = -i\hbar\nabla_R S(R). \qquad (4)$$

where $\mathbf{R} = \mathbf{R}_S - \mathbf{R}_V$ and $S(R)$ is the overlap integral between $\varphi_s(\mathbf{r})$ and $\varphi_\nu(\mathbf{r})$.

Using Eqns. (1), (3), and (4), we obtain from Eqn. (2) the relation between the parameter $h_{\nu s}$ of the Hamiltonian and the matrix element $\mathbf{p}_{\nu s}$ of the momentum:

$$i\hbar\,\mathbf{p}_{\nu s} = h_{\nu s}(\mathbf{R}_\nu - \mathbf{R}_s),$$

or, finally, we obtain the following formula for the resonance integral:

$$h_{\nu s} \equiv \beta_{\nu s}(R) = \frac{\hbar^2}{m}\frac{1}{R}\frac{dS}{dR}, \quad R = |\mathbf{R}_\nu - \mathbf{R}_s|. \qquad (5)$$

The Slater functions with Z_{eff} = 3.18 for carbon and Z_{eff} = 3.8 for nitrogen as well as the Hartree–Fock functions for these atoms were used as the atomic $2p_z$ functions from which the $\varphi_s(\mathbf{r})$ functions were constructed with the aid of Lowdin's orthogonalisation procedure[15]. The results of the calculation (together with certain refinements[16]) for the benzene and ethylene bonds and the aniline CN bond are presented in Table 1. It was found that the observed βCN and βCC are close to the empirical values determined from the absorption spectra.

Linderberg's scheme for the calculation of resonance integrals has been used in calculations on a number of molecules with heteroatoms[17,18]. It was found that the results of the calculation agree well with experiment and are close to the results obtained in calculations employing the usual parametrisation schemes[19].

We believe that the derivation of relations between theoretical parameters, such as the Linderberg relation (5), constitutes a fruitful procedure for the development of the theory and for the achievement of its internal self-consistency.

We may note certain inaccuracies in the derivation of Eqn. (5), which was taken from Linderberg's paper[14]. According to this derivation, the overlap integral S is

calculated with the orthogonal functions $\varphi_p(\mathbf{r})$. Therefore the overlap integral $S = 0$ for $\varphi_s(\mathbf{r})$ and $\varphi_p(\mathbf{r})$ ($s \neq p$), which does not prevent the derivative dS/dR from being non-zero. However, the functions $\varphi_p(\mathbf{r})$ are made up by the superposition of non-orthogonal atomic functions $\chi_i(\mathbf{r})$ of the $2p_z$ type localised at atoms i (see the previous review[1] for more detail):

$$\varphi_p(r) = \sum_i \chi_i(r)\, c_{ip}\,.$$

Table 1. The resonance integrals calculated by Linderberg's method[14] [the upper figures represent the value calculated using Slater's functions and the lower figures the values obtained with the Hartree–Fock functions for the C and N atoms. The last columns list the resonance integrals ($-\beta$) for benzene obtained by an improved calculation using Slater's functions with different Z (Jug[16])].

Molecule	Designation of resonance integral	C-C bond			
		R, Å	$-\beta$ (R), eV	$Z = 3.18$	$Z = 2.58$
Ethylene	β_{12}	1.34	2.685 2.588		
Benzene	β_{12}	1.4	2.42 2.38	2.27	2.47
	β_{13}	2.42	0 0	—0.05	—0.02
	β_{14}	2.8	0.14 0.19	0.08	0.13
		CN bond			
Aniline	β CN	1.47	1.75 1.77		

Therefore in Eqns. (3) and in subsequent treatment $\mathbf{R_q}$ is not a coordinate of the atom q. Formally $\mathbf{R_q}$ is a diagonal matrix element, expressed as a function of $\mathbf{r}$, calculated using the functions $\varphi_q(\mathbf{r})$:

$$\mathbf{R}_q = \int \varphi_q(\mathbf{r})\, \mathbf{r}\, \varphi_q(\mathbf{r})\, d\mathbf{r}\,.$$

On the other hand, the true coordinate of the atom q, which will now be designated by $\mathbf{R}^0_q$, is equal to the diagonal matrix element expressed as a function of $\mathbf{r}$, using the functions $\chi_q(\mathbf{r})$:

$$\mathbf{R}^0_q = \int \chi_q(\mathbf{r})\, \mathbf{r}\, \chi_q(\mathbf{r})\, d\mathbf{r},$$

and it is readily seen that $\mathbf{R_q} \neq \mathbf{R}^0_q$. Furthermore, Eqn. (3) for the operator $\mathbf{r}$ is inaccurate also because non-zero matrix elements with the off-diagonal indices p and q, expressed in terms of the functions $\varphi_p(\mathbf{r})$, were neglected in its formulation. The exact formula for the operator $\mathbf{r}$ is

$$\mathbf{r} = \sum_{pq,\eta} \mathbf{R}_{pq} c^+_{p\eta} c_{q\eta}, \quad \mathbf{R}_{pq} = \int \varphi_p(\mathbf{r})\, \mathbf{r}\, \varphi_q(\mathbf{r})\, d\mathbf{r}.$$

These inaccuracies were corrected in subsequent studies†, but we shall not consider this problem in greater detail‡ in view of the fairly cumbersome nature of the expressions.

†In Linderberg's[20] and Jug's[21] studies.

‡Various aspects of the employment and interpretation of Eqn. (5) are discussed in a recent study[22].

Linderberg's idea, employing the fundamental relation between the coordinate and the momentum, appears to us more attractive and fruitful than direct calculation of $\beta_{\mu\nu}$ with specified functions and potentials of the Goeppert–Mayer and Sklar type (see, for example, Yoshida and Kobayashi[6] whose calculated $\beta_{\mu\nu}$ are very close to the semiempirical values). At the same time, we believe that in the future it will be necessary to compare carefully these two methods for the calculation of $\beta_{\mu\nu}$.

3. PROBLEMS OF THE INTERACTION OF π ELECTRONS WITH THE σ SKELETON

The problem of the interaction of π and σ electrons have always been of interest for the semiempirical theory of conjugated systems, since the limits of the applicability of the π-electron theory are then elucidated and the significance of the semiempirical formulae employed is discovered.

a. The Mixing of One-Electron σ and π Energy Levels in Conjugated Molecules

Studies have been published recently indicating the mixing of one-electron σ and π energy levels in conjugated systems, which seemingly constitutes evidence against the π-electron approximation. Thus analysis of experiments on the photoionisation of benzene[23,24] showed that a filled σ energy level is located in benzene between filled π levels. A similar pattern with mixing of σ and π energy levels follows also from numerous calculations on various molecules in terms of the SCF approximation, which have given rise to a lively discussion[25].

Many investigators found the reports of such mixing of σ and π levels very unexpected, because all the properties of conjugated systems, including absorption spectra, had been satisfactorily explained hitherto with the aid $\pi \rightarrow \pi^*$ transitions alone. All previous experience in the quantum chemistry of conjugated system could be reconciled with the mixing of σ and π energy levels only by postulating a weak interaction between the σ- and π-electron systems. This was in fact found to be the case.

A study of transition probabilities by the Hückel method for all the valence electrons of naphthalene and anthracene[25] showed that the transition probabilities (oscillator strengths) for the $\sigma \rightarrow \pi^*$ transitions are smaller by 3–4 orders of magnitude than for the $\pi \rightarrow \pi^*$ transitions. In $\sigma \rightarrow \pi^*$ transitions the emission is polarised perpendicular to the plane of the conjugated molecules, because only matrix elements of the type[25]

$$I = \langle \varphi_{s_i} | z | \varphi_{z_i} \rangle\,,$$

where φ_{s_i} and φ_{z_i} are $2s$ and $2p_z$ functions of the atom i, contribute to the transition moment (in terms of the one-centre approximation). The quantity $I \leqslant a_0$ (a_0 is the Bohr radius) is in fact independent of the molecular size and the number of atom i.

In $\pi \rightarrow \pi^*$ transitions the emission is polarised in the molecular plane and matrix elements of the type

$$X_i = \langle \varphi_{z_i} | x | \varphi_{z_i} \rangle, \quad Y_i = \langle \varphi_{z_i} | y | \varphi_{z_i} \rangle$$

contribute to the transition amplitude. X_i and Y_i are essentially coordinates of the atoms i, so that they are comparable to the dimensions of the conjugated molecule, exceeding appreciably the value of a_0.

There is yet another cause of the decrease of the probability of the $\sigma \rightarrow \pi^*$ transitions. When the two molecular orbitals involved in the $\sigma \rightarrow \pi^*$ transition are formulated:

$$\psi^\sigma = \sum_i c_i^\sigma \varphi_{s_i} + \text{члены с } \varphi_{x_i}, \varphi_{y_i}$$

$$\psi^\pi = \sum_i c_i^\pi \varphi_{z_i},$$

the $\sigma \rightarrow \pi^*$ transition amplitude becomes

$$\langle \psi^\sigma | z | \psi^\pi \rangle = \langle \varphi_{s_i} | z | \varphi_{z_i} \rangle \sum_i c_i^\sigma c_i^\pi = I \sum_i c_i^\sigma c_i^\pi. \quad (6)$$

It was discovered that this amplitude is small also because the coefficients c_i^σ are as a rule small for the highest occupied σ orbitals.

This analysis shows that the lines of the $\sigma \rightarrow \pi^*$ transitions must be much weaker than those of the $\pi-\pi^*$ transitions, which predominate in the experimental spectrum. The different polarisations of emission in $\pi \rightarrow \pi^*$ and $\sigma \rightarrow \pi^*$ transitions may assist the observation of weak $\sigma \rightarrow \pi^*$ transitions. Furthermore, it is quite likely that ionisation from filled σ orbitals was indeed observed in the photoionisation of benzene and other molecules[23,24,26].

We may note that, for small conjugated molecules such as ethylene and formaldehyde, $\sigma \rightarrow \pi^*$ transitions (and $\pi-\sigma^*$ transitions) are just as intense as the $\pi \rightarrow \pi^*$ transitions. This also follows from Eqn. (6), since in ethylene, for example, the coefficients c_i^σ are relatively large[25].

b. Calculations on Non-planar Conjugated Systems

The interaction of σ and π electrons becomes significant when non-planar conjugated systems are considered. So far very few studies have been devoted to calculations on the electronic structures of such systems. For example, stilbene and diphenylbutadiene molecules, in which the coplanarity breaks down as a result of rotation about the central C–C bond of one part of the molecule relative to the other by an angle α, have been considered[27,28]. In the calculation by the PPP method the usual parameters were used and only the resonance integral of the central bond was multiplied by $\cos\alpha$. A good agreement has been obtained[28] with the experimental position of the first singlet energy level, while in another study[27] not even a qualitative explanation of the energy level shifts on passing to a non-planar system was obtained.

We believe that the problem of the parameters for non-planar conjugated systems cannot be solved by a simple alteration of the resonance integral for one bond. The interactions between non-bonded atoms in the molecule become significant in non-planar systems[28] and it is necessary to take into account more accurately the repulsion of the positively charged σ skeleton[29]. In non-planar systems the π-electron orbitals are no longer orthogonal with respect to the orbitals of the electrons in the σ skeleton. Therefore, in order to consider π electrons separately, as before, i.e. in order to retain the π-electron approximation, it is necessary to carry out the orthogonalisation (for example, by Löwdin's method[15]) of the π-electron orbitals in the non-planar configuration with respect to the orbitals of the new σ skeleton. Only then is it possible to understand how the effective parameters of the model π-electron Hamiltonian are changed relative to the planar case.

c. The Hyperfine Structure of the ESR Spectra and the McConnell Formula

The interaction of σ and π electrons can be readily observed by ESR (and NMR) methods, when a spin density ρ^π appears in the π-electron system. The spin density ρ^π in π-electron radicals, radical-ions, or triplet states of conjugated molecules polarises the electrons of the σ skeleton and leads to the appearance of a spin density ρ^σ in the σ-electron system. As a result of the contact interaction of ρ^σ with the magnetic moments of the nuclei in the conjugated system (when these nuclei have magnetic moments), a hyperfine structure (HFS) appears in the ESR method[30], the additional (hyperfine) splitting of the ESR Zeeman line by each magnetic nucleus is specified by the hyperfine splitting constant. In the case of hydrocarbons the HFS of the ESR spectra depends on the proton splittings a_{H_i} in the Ci–Hi bonds.

According to the theory of McConnell and Chesnut[31], the splitting a_{H_i} is proportional to the exchange integral calculated using the $2p_z$ functions (φ_{z_i}) of the atoms Ci and the functions of the ground (Φ_σ) and excited (Φ_{σ^*}) states of the electrons in the Ci–Hi bond:

$$a_{H_i} = \text{const} \cdot \langle \Phi_\sigma \varphi_{z_i} | \Phi_{\sigma^*} \varphi_{z_i} \rangle. \quad (7)$$

Making certain assumptions, the relation known as the McConnell formula was obtained from Eqn. (7):[31]

$$a_{H_i} = Q \rho_i^\pi, \quad (8)$$

where ρ_i^π is the π-electron spin density at the atom C_i linked to Hi and Q is a constant. Eqn. (8) made it possible to employ the results of the calculation of ρ_i^π in the interpretation of ESR spectra. As a result, ESR became one of the procedures for the investigation of the electronic structures of conjugated systems.

Subsequently analysis of the systematic deviations from McConnell's formula [Eqn. (8)] for hydrocarbon radical-cations and radical-anions led to a refinement of this formula[32] by the introduction of a relation between a_{H_i} and the π-electronic charge q_i of the atom Ci:

$$a_{H_i} = (Q' + Kq_i)\rho_i^\pi. \quad (9)$$

This relation, known as the Colpa–Bolton formula, was obtained from Eqn. (7) on the assumption that the charge q_i influences the σ orbital of the C–H bond[32].

Detailed analysis of the approximations leading to the McConnell formula [Eqn. (8)] showed[33] that the formula is correct only in the zeroth approximation. A more accurate formula for a_{H_i} includes both the diagonal elements of the spin density matrix $Q_{ii} = \rho_{ii}^\pi$ and the off-diagonal elements Q_{ij} ($Q_{ij} = c_i^0 c_j^{0*}$, where c_j^0 is a coefficient of the jth atomic orbital for the unpaired electron molecular orbital). This more general formula is[33]

$$a_{H_i} = -26{,}07 Q_{ii} - 10.40 \sum_{k\ (i\ \text{neighbours})} Q_{ik}\ (\text{gauss}). \quad (10)$$

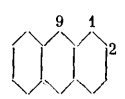
A similar formula was proposed for a_{H_i} even earlier[34].

The results of the calculation of a_{H_i} by Eqn. (10) are presented in Table 2, which shows that Eqn. (10) represents satisfactorily the changes in a_{H_i} on passing from a cation to an anion and therefore constitutes a generalisation of both the McConnell [Eqn. (8)] and Colpa–Bolton [Eqn. (9)] formulae.

Nevertheless, the McConnell and Colpa–Bolton formulae are widely used in semiempirical calculations, because

they make it possible to determine with satisfactory accuracy (to within about 10–15%) both the relative and absolute HFC constants not only for protons but also for other nuclei (^{13}C, ^{14}N, etc.)[35]. Eqns. (8) and (9) are usually treated as empirical relations with the constants Q, Q', and K.

Table 2. The hyperfine splittings a_{H_i} for the positive and negative ions of naphthalene and anthracene[33].

Molecule	Sign of ion	No. of atom	a_{H_i}, G expt.	a_{H_i}, G Eqn.(10)
	−	1	−4.90	−5.11
		2	−1.83	−1.78
	+	1	−5.54	−5.64
		2	−2.06	−1.89
	−	1	−2.74	−2.74
		2	−1.51	−1.35
		9	−5.56	−5.45
	+	1	−3.11	−2.80
		2	−1.40	−1.24
		9	−6.56	−6.68

Relations between the experimental constants $a_{H_i}^{exp}$ and $a_{H_i}^{calc}$ calculated by Eqns. (8) and (9) for a large number of π-electron radicals have been analysed[36]. The ρ_i^π were calculated by ten different methods, optimum values of the constants Q, Q', and K being selected for each method. It was found that all the methods for the calculation of ρ_i^π yield a good agreement between $a_{H_i}^{exp}$ and $a_{H_i}^{calc}$. The average discrepancies are $\leqslant 1$ G, although in a few instances they may reach 2–3 G. However, the optimum constants Q, Q', and K depend markedly on the method of calculation (Table 3).

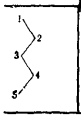
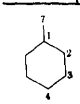
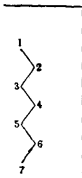
Table 3. The optimum constants Q' and K (gauss) in the Colpa–Bolton formula [Eqn. (9)] for different methods of calculating spin densities[36].

Method of calculation of spin density	Q'	K
Hückel	35.62	16.78
Hückel + CI (Ref.37)	31.50	16.86
McLachlan	25.05	18.37
UHF	20.43	10.60
UHF with annihilation of the quartet	28.50	12.66

It was also noted[36] that the optimum constants depend on the number of neighbours of the carbon atom and on the sign of its spin density. These fine features are not taken into account in the McConnell formula [Eqn. (8)]. A characteristic example is the benzyl radical, where the ratio $a_{H_2}/a_{H_4} < 1$ (in contrast to the McConnell formula), while according to all the methods of calculation employed, the ratio of the spin densities of the carbon atoms $\rho_2^\pi/\rho_4^\pi \geqslant 1$ (Table 4).

A non-empirical calculation of the electronic structure of the benzyl radical in terms of the SCF approximation taking into account all the electrons (σ and π), carried out by Kruglyak et al.[44], yielded directly the spin densities of the *ortho*- and *para*-protons. The ratio of these densities $\rho_{H_2}^\sigma/\rho_{H_4}^\sigma < 1$, in agreement with experiment, while the ratio of the spin densities in the π-electron system was still incorrect: $\rho_2^\pi/\rho_4^\pi \gtrsim 1$. The calculation showed that the $\sigma \rightarrow \pi$ interaction had an insignificant influence on the π orbitals and on the distribution of spin density in the π-electron system. It was therefore concluded that the McConnell formula is inadequate for the calculation of a_{H_i} for the benzyl radical[44].

Table 4. Spin densities calculated by different methods[38].

Radical	No. of atom	Method of calculation: SCF	SCF + singly excited configurations	full CI[c]	UHF	UHF with annihilation	Hückel	McLachlan	$\lvert a_{H_i}\rvert$ (expt.) G
	1	0.253	0.330[a]	0.413	0.553	0.387	0.333		8.99[e]
	2	0	−0.092	−0.140	−0.314	−0.096	0		2.65
	3	0.494	0.525	0.452	0.523	0.418	0.333		13.40
	7	0.791	0.706[b]	0.715	0.760	0.711	0.571	0.770	16.36[d]
	1	0	−0.095	−0.110	−0.197	−0.062	0	−0.102	—
	2	0.081	0.174	0.185	0.268	0.163	0.143	0.161	5.14
	3	0	−0.058	−0.070	−0.172	−0.054	0	−0.063	1.75
	4	0.046	0.156	0.165	0.238	0.134	0.143	0.137	6.14
	1			0.325	0.356		0.25		
	2			−0.117	−0.096		0		
	3			0.367	0.295		0.25		
	4			−0.150	−0.110		0		

[a] According to Hinchliffe[39].
[b] According to Kuprievich et al.[40].
[c] According to Amos and Burrows[41].
[d] According to Trinajstić[42].
[e] According to Nowakowski[43].

4. THE DISTRIBUTION OF SPIN DENSITY IN RADICALS

a. The Hückel Method

The application of the Hückel method makes it possible to obtain a qualitatively correct distribution of spin density in the radical[45–48]. In combination with the McConnell formula, the Hückel method permits the interpretation of fairly complex ESR spectra, which may have an unresolved HFS for a solid phase. In the interpretation of such spectra of the radicals of certain acetylene derivatives the necessity to take into account the real bond lengths in the radicals in order to obtain a correct spin density distribution was demonstrated for the first time[48]. The "bond length–bond order" formula and the linear relation between the resonance integral β and the bond length, $\beta = \beta_0 + \delta(R - R_0)$, were used for this purpose in the

Hückel approximation. It was found that the exponential relation [49]

$$\beta = \beta_0 \exp[a(R_0 - R)] \qquad (11)$$

frequently leads to an incorrect spin density distribution in radicals with long and short bonds (from 1.45 to 1.20 Å). For example in the radical $C_{(1)}H_2-C_{(2)}\equiv C_{(3)}H$ the ratio of the spin densities at the $C_{(1)}$ and $C_{(3)}$ atoms is

$$\rho_1^\pi/\rho_3^\pi = (\beta_{23}/\beta_{12})^2$$

and Eqn. (11) leads to a very high value of this ratio, in conflict with experiment [48]. The region of applicability of Eqn. (11) is limited to small changes in bond lengths, were the exponential relation barely differs from a linear relation.

For aromatic radicals, where all the $R \simeq R_0 = 1.4$ Å, the influence of differing bond lengths on the spin density distribution was not studied systematically. Nevertheless allowance for the real geometry of the radicals can alter the calculated ρ_i^π by 5–10%. This remark applies not only to the Hückel method but also to other methods in which the interaction between electrons is taken into account.

The Hückel method yields satisfactory relative values of not unduly small spin densities ρ_i^π, but fails to predict small (positive and negative) values of ρ_i^π. A negative spin density appears as a result of the repulsion of π electrons with opposed spin projections, which can accumulate at different atoms and lead to a pattern of alternating signs of the spin density at neighbouring atoms. Therfore, in order to describe such spin density distributions, it is necessary to take into account explicitly the interaction of π electrons. The changes in spin density $\Delta\rho_i^\pi$ due to inclusion of the π-electron interaction are as a rule small ($|\Delta\rho_i^\pi| < 0.1$), which accounts for the relative success of the Hückel method.

b. Methods with Different Molecular Orbitals for Different Spins. Projection of the Wave Functions on to States with a Correct Total Spin

In order to take into account the electron interactions, it is reasonable to employ the SCF method with different molecular orbitals for electrons having different spins [50–55]. In this method two electrons with opposite spins do not occupy the same molecular orbital (as in the simple SCF method) but two different molecular orbitals. As a result, an electron having one spin is largely located at one set of atoms in the molecule, while an electron having another spin is located at another set of atoms. Owing to the decrease of the Coulomb interaction energy of these electrons, the total energy of the molecule is lower than in the simple molecular orbital method [50,51]. The method using different molecular orbitals for different spins is equivalent to the method of interacting configurations and is used to calculate the electronic structures of conjugated molecules [56]. Its application to conjugated radicals provides a natural explanation of the appearance of negative spin densities in the system.

One of the variants of this method is called the unrestricted Hartree–Fock method (UHF). The wave function of the radical in the UHF method (one Slater determinant of molecular spin orbitals) consists of a superposition of functions for different spins and can be represented as follows:

$$\Phi = \sum_{S=1/2}^{N/2} a_S \Phi_{1/2}^S , \qquad (12)$$

where $\Phi_{1/2}^S$ are orthonormalised functions which are the eigenfunctions of the operator of the square of the total spin $\hat{S}^2$ with eigenvalues $S(S+1)$ and the operator of the projection of the total spin $\hat{S}_z$ with $S_z = 1/2$. In order to separate the components having the spin $S = 1/2$ (the radicals have a doublet ground state) from Eqn. (12), a fairly cumbersome spin projection operation is necessary. The application of the operator [57]

$$O_{1/2} = \prod_{k\,(\neq 1/2)}^{N/2} [k(k+1) - \hat{S}^2]$$

to function (12) eliminates all terms except $a_{1/2}\Phi_{1/2}^{1/2}$. The operator $\hat{S}^2$ for a system of N electrons is

$$\hat{S}^2 = -\frac{1}{4}N(N-4) + \sum_{i<j}^{N} P_{ij}^\eta,$$

where P_{ij}^η interchanges the spin coordinates of the electrons i and j.

In view of the complexity of the projection operation, it has been suggested [58,59] that one excludes from function (12) only the quartet component ($S = 3/2$), which apparently makes the next highest contribution to the function Φ after the component with $S = 1/2$. The quartet is annihilated by the operator

$$\hat{A} = \hat{S}^2 - 15/4.$$

The closeness of the average value of $\langle\Phi|S^2|\Phi\rangle$ to $3/4 = S(S+1)$ for $S = 1/2$ can serve as a criterion of the closeness of the function Φ to the doublet state. Usually $\langle\Phi|S^2|\Phi\rangle > 3/4$ and the annihilation of the quartet reduces the average value of $\hat{S}^2$. However, it has been shown [60] that in certain cases the mean $\hat{S}^2$ increases after the annihilation of the quartet. The observed ineffectiveness of the annihilation of the quartet depends on the choice of the parameters of the PPP Hamiltonian [60].

The UHF method and the UHF method with partial annihilation are fairly complex and the results obtained for the distribution of spin density are so far only qualitatively consistent with one another and with the results of calculations with complete allowance for the interaction of π electrons (Table 4).

In certain cases, particularly in analytical calculations for large molecules with a regular structure, another technique of projecting the wave function on to a state with a correct total spin is more convenient [61–63]. This technique employs the operator of a finite rotation in spin space by the Eulerian angles $\tilde{\alpha}$, $\tilde{\beta}$, and $\tilde{\gamma}$:

$$\hat{R} = \exp(-i\hat{S}_z\tilde{\alpha}) \cdot \exp(-i\hat{S}_y\tilde{\beta}) \cdot \exp(-i\hat{S}_z\tilde{\gamma}).$$

The action of the operator $\hat{R}$ on the function Φ_m^S, the eigenfunction $\hat{S}^2$, and $\hat{S}_z$ (with a spin S and its projection $S_z = m$) is defined by the formula

$$\hat{R}\Phi_m^S = \sum_{n=-S}^{S} D_{nm}^{(S)}(\tilde{\alpha}\tilde{\beta}\gamma)\,\Phi_n^S, \qquad (13)$$

where $D_{nm}^{(S)}(\tilde{\alpha}\tilde{\beta}\tilde{\gamma})$ is the Wigner D-function [64]. D-Functions possess the property of orthogonality, which is important for our problem:

$$\int_0^{2\pi} d\tilde{\alpha} \int_0^{\pi} d\tilde{\beta}\sin\tilde{\beta} \int_0^{2\pi} d\tilde{\gamma}\, D_{nm}^{(S)}(\tilde{\alpha}\tilde{\beta}\tilde{\gamma})\, D_{n'm'}^{(S')*}(\tilde{\alpha}\tilde{\beta}\tilde{\gamma}) = \frac{8\pi^2}{2S+1}\delta_{SS'}\delta_{nn'}\delta_{mm'}. \qquad (14)$$

We allow the operator $\hat{R}$ to act on the function Φ [Eqn. (12)]. Using Eqn. (13), we obtain

$$\hat{R}\Phi = \sum_{S_1=1/2}^{N/2} a_{S_1} \sum_{n=-S_1}^{S_1} D_{n1}^{(S_1)}(\tilde{\alpha}\tilde{\beta}\tilde{\gamma})\,\Phi_n^{S_1} . \qquad (15)$$

We multiply both sides of Eqn. (15) by $D^{(S)}_{S_{Z1/2}}(\tilde{\alpha}\tilde{\beta}\tilde{\gamma})$ and integrate with respect to all the angles, as in Eqn. (14); then, using Eqn. (14), we obtain

$$a_S \Phi^S_{S_z} = \frac{2S+1}{8\pi^2} \int_0^{2\pi} d\tilde{\alpha} \int_0^{\pi} d\tilde{\beta} \sin\tilde{\beta} \int_0^{2\pi} d\tilde{\gamma} D^{(S)*}_{S_z 1/2}(\tilde{\alpha}\tilde{\beta}\tilde{\gamma}) \hat{R}\Phi \ . \qquad (16)$$

In order to isolate the doublet component, it is necessary to put $S = S_Z = 1/2$. In principle, Eqns. (16) can be used also in calculations on molecules employing different variants of the method with different molecular orbitals for different spins (see, for example, Refs. 61–64).

c. McLachlan's Method

Since the changes in the spin densities $\Delta\rho_i^{\pi}$ due to the inclusion of the interelectron interaction in polyatomic radicals are small compared with unity, one can employ perturbation theory in order to take into account the effect of electron interactions on the distribution of spin density. Instead of a complete solution of the SCF equations in the UHF method, McLachlan [65] employed the perturbation theory and obtained an approximate formula for the spin density. The spin density of the π electrons in the atom i is given by the formula [65]:

$$\rho_i = \rho_i^{\circ} - \lambda \sum_k \pi_{ik} \rho_k^{\circ}, \qquad (17)$$

where π_{ik} is the coefficient of the mutual polarisability of the atoms i and k, $\rho_i^{\circ} = |c_i^{\circ}|^2$ is the spin density calculated by the Hückel method (c_i° is the coefficient of the molecular orbital of the unpaired electron of the atom i in the Hückel method), and $\lambda \simeq \gamma_{11}/2|\beta| \simeq 1.2$ is an empirical constant.

There are several modern schemes based on the McLachlan method for hydrocarbons [43] which lead to a satisfactory agreement with experiment when McConnell's formula is used to calculate the hyperfine splittings.

McLachlan's method has been used successfully to calculate the proton, ^{13}C, and ^{14}N splittings in compounds with heteroatoms, In order to calculate the ^{13}C and ^{14}N splittings, McConnell's formula [Eqn. (8)] was modified by adding contributions proportional to the spin densities at the neighbouring atoms [45–47]. For example the formula

$$a_N = 23.1\rho_N - 6.3\rho_C \qquad (18)$$

is used to calculate the hyperfine splitting constant for nitrogen in the cyano-group C≡N. Similar formulae are used also for other hyperfine splittings [66]. Empirical formulae of type (18) are very similar to Eqn. (10), which constitutes a generalisation of the McConnell and Colpa–Bolton formulae for hydrocarbons: the mutual influence of atoms is taken into account in these formulae.

A paradoxical situation existed for some time: calculations of hyperfine splittings for compounds with heteroatoms by McLachlan's method [45–47] agreed better with experiment than calculations by the UHF method or the SCF method in the multi-configuration approximation [39], despite the fact that McLachlan's method is an approximation to the UHF method.

The situation became clarified after the calculation by the UHF method (with annihilation of the quartet) using the parameters of the PPP Hamiltonian which reproduced satisfactorily the excitation and ionisation energies of the corresponding molecules [66]. It was found that in this case the agreement with experiment is better than in McLachlan's method: the average deviation from the experimental values of the hyperfine splitting proved to be ±0.59 G, while in McLachlan's method the average deviation was ±0.86 G. [46,47] In this calculation [66] new values of the parameters in the formulae for the splittings were selected. The high effectiveness of the annihilation of the quartets was noted, probably by virtue of a successful choice of the PPP Hamiltonian parameters: the mean values of $\hat{S}^2$ after annihilation differed from the exact value for the doublet (0.75) only in the third decimal place [66]. This example yet again demonstrates the necessity for employing sets of parameters adjusted for consistency in semiempirical calculations.

d. Calculations with Partial and Full Configuration Interaction

Kuprievich et al. [40] calculated the spin structure of the benzyl radical by the SCF method with subsequent inclusion of singly excited, doubly excited, ect. configurations until all the configurations (404) for the ground state were included, i.e. complete account was taken of the interaction of π electrons. The results of the calculation are presented in Table 5, which shows that the spin densities calculated taking into account all possible configurations are reproduced with satisfactory accuracy (to within ≤ 10%) when account was taken of singly excited configurations only. In this connection we may note the satisfactory qualitative and quantitative agreement with experiment obtained in SCF calculation of the spin structure of radicals which include the configurations of the ground state and all singly excited configurations [37,39]. We may note that in the above studies use was made of both molecular orbitals adjusted for consistency and of Hückel molecular orbitals, which are fairly close to one another and which led to similar spin densities.

Table 5. The spin structure of the benzyl radical in terms of the configuration interaction method [40].

No. of atom	Spin densities			
	ground state (GS) and single excitations (15 configurations)	GS and single and double excitations (89 configurations)	GS and single, double, and triple excitations (239 configurations)	full configuration interaction (404 configurations)
7	0.706	0.741	0.722	0.724
1	−0.095	−0.100	−0.110	−0.112
2	0.174	0.165	0.183	0.183
3	−0.058	−0.058	−0.069	−0.070
4	0.156	0.146	0.161	0.161

Calculations taking into account all possible excited configurations (full configuration interaction) have been carried out also in other studies [41]. The spin densities calculated for certain radicals by different methods are compared in Table 4 with the values calculated allowing for the full configuration interaction.

5. CERTAIN RECENT METHODS FOR THE CALCULATION OF THE ELECTRONIC STRUCTURES OF MOLECULES OTHER THAN THE PARISER–PARR–POPLE METHOD

a. The Method of "Molecules in Molecules"

In calculations on large conjugated molecules consisting of several fragments linked by one or two bonds the method of "molecules in molecules" (MIM) has been used successfully. As a rule, the absorption spectra of such a molecule contain lines and bands characteristic of the isolated fragments. This serves as a "criterion" for the application of the MIM method.

In the MIM method one calculates initially (the electronic structures of the individual fragments (for example by the PPP method). The wave function of the entire molecule is constructed as a superposition of the product of the wave functions of the fragments, the ground and several excited states of each fragment and the state with charge transfer from one fragment to another being considered. The total number of configurations of this kind involved in the construction of the wave function is much smaller than in calculations on the molecule by the PPP method. The results of the calculation agree with experiment just as well as the complete calculation by the PPP method. This was demonstrated, for example, in the calculation on decacyclene (36 atoms), which consists of three fragments—acenaphthylene molecules (12 atoms)[67]. The general postulates of the theory of the MIM method have been described together with a brief survey of the literature by von Niessen[68].

The MIM method has been used[69] for calculations on the $S-T$ and $T-T$ transitions in aromatic molecules. In these calculations the experimental energies were used for the fragments (for the corresponding matrix elements of the Hamiltonian) instead of the energies calculated by the PPP method, as in the study of Brugmann et al.[67] This led to a satisfactory agreement with experiment. Thus use was made of the old idea put forward by Moffitt[70,71] (on which the method of "atoms of molecules" is based), who employed the experimental energies for the atoms (O, N, etc.) in calculations on the molecules (O_2, N_2, etc.).

b. The Random Phase Approximation and the Multi-configuration Interaction Method

Mestechkin[72–74] used successfully the approximation of random phases (in the semiempirical version for conjugated systems using the technique of density matrices) to calculate the electronic structures of condensed aromatic molecules[72–74]. A special parametrisation scheme was used which, as we have seen, is reasonable for various methods in the semiempirical theory. As a result, it was possible to calculate the positions of the triplet levels to within about 0.1 eV (for the lowest levels) and with a somewhat poorer accuracy for the highest levels.

In the random phase approximation configurations are taken into account in a compact form and the configurations themselves do not arise explicitly. If the same configurations were considered explicitly, then in principle the calculation would be more accurate, although it would be much more laborious and time consuming.

The condition for the applicability of the random phase approximation is the smallness of the relative changes in the π-electron density at the atom on excitation of the molecule, namely[75]

$$\Delta q_l/q_l \ll 1 \quad \text{or} \quad \Delta q_l \ll 1\,, \tag{19}$$

since the π-electron densities at atoms in conjugated molecules are $q_l \simeq 1$. The greater the charge redistribution in the molecule, i.e. the greater the Δq_l, the higher the excitation energy. Therefore the accuracy of the random phase approximation falls for high excitation energies. A similar criterion of the applicability of the random phase approximation (spin densities much less than unity) exists also for triplet excitations[75].

The random phase approximation has so far been rarely used to investigate conjugated systems[72–80]. Therefore the scope of the method has still not been fully explored.

The same remark holds also for the multi-configuration interaction method (MCI). In the MCI method the wave function of the system Φ is constructed as a superposition of several (n) configurations Φ_i (each configuration consists of a Slater determinant comprising molecular spin orbitals):

$$\Phi = \sum_{i=1}^{n} c_i \Phi_i.$$

The coefficients c_i and the coefficients of the linear combinations of molecular orbitals used to construct the Φ_i are found by a special procedure. This yields both the function of the ground state (with the coefficients c_i^0) and the functions of the n-1 excited states (with the coefficients c_i^k, $k = 1, 2, \ldots, n-1$).

The MCI method is used to calculate various molecular characteristics, including the distributions of spin densities in radicals[38]. Different versions of the MCI method have been developed by Japanese[81] and Soviet[82] investigators.

The MCI method resembles somewhat the MIM method and the random phase approximation. As in the random phase approximation, account is taken in the MCI method of the interaction of π electrons and of excited configurations, but the contributions of these configurations are calculated exactly and the number of configurations is small; as in the MIM method, the configurations are selected on the basis of simple considerations (for example, on the basis of their energies, on symmetry grounds, etc.).

c. The Method of Full Configuration Interaction

Calculations with full allowance for the interaction of π electrons, with full configuration interaction, occupy a special place in the theory of conjugated systems. If we are interested in all the energy levels and all the properties of the system, the method of full configuration interaction is equivalent to the problem of the determination of these properties. Then, using the same effective parameters of the model π-electron Hamiltonian to describe all the properties of the molecule, we can detect the inaccuracies of the π-electron approximation itself. Calculations with full configuration interaction are interesting not only as a method for the complete investigation of the system properties but mainly because such calculations reveal the scope of various approximate methods.

The method of calculation with full configuration interaction proposed by the present authors[75,83,84] is very convenient for the ZDO approximation when the PPP

Hamiltonian is used. In this method [84] the wave function Φ for the system of N electrons is expressed in the form

$$\Phi = \sum_{i=1}^{l_S^N} \psi_i(\mathbf{r}_1, \mathbf{r}_2, \ldots, \mathbf{r}_N)\theta_i(\eta_1\eta_2 \ldots \eta_N),$$

where the spin functions θ_i are defined by the spin state of the system and the coordinate functions ψ_i are expressed as an expansion in products of the atomic orbitals $\varphi_n(\mathbf{r})$:

$$\psi_i = \sum_{n_1=1}^{K}\sum_{n_2=1}^{K} \ldots \sum_{n_N=1}^{K} c_i(n_1 n_2 \ldots n_N)\varphi_{n_1}(\mathbf{r}_1)\varphi_{n_2}(\mathbf{r}_2) \ldots \varphi_{n_N}(\mathbf{r}_N),$$

where K is the number of different atomic orbitals [the dimension of the basis set $\varphi_n(\mathbf{r})$]:

$$l_S^N = \frac{(2S+1)\cdot N!}{(N/2+S+1)!\,(N/2-S)!},$$

where S are the spin states.

The requirement that Φ be antisymmetric with respect to interchange of the particles (the Pauli principle) and allowance for molecular and spin symmetry decrease the number of unknown coefficients $c_i(n_1 n_2 \ldots n_N)$ and establish simple linear relations between the latter. These relations reduce the large number of coefficients $c_i(n_1 n_2 \ldots n_N)$ to a comparatively small number M of unknown coefficients which can be found from the Schrödinger equation $H\Phi = E\Phi$ or $H\psi_i = E\psi_i$, where H is the Hamiltonian of the system and E the total energy.

The required matrix $H_{\mu\nu}$ for the secular equation can be found in the simplest possible way by a sequence of simple operations [84]. The degree of this secular equation, obtained as a result of the variation of the average total energy with respect to M unknown coefficients, is equal to the number of all the configurations μ, ν, ..., possible for the given state. A characteristic feature of this method of allowance for all configurations [84] is that, owing to the ZDO approximation, the PPP Hamiltonian has the following features: (1) the off-diagonal elements $H_{\mu\nu}$ consist of simple linear combinations of resonance integrals β_{mn} or are zero; (2) the number of zero elements $H_{\mu\nu}$ is several times greater than that of the non-zero elements; (3) the diagonal elements $H_{\mu\mu}$ consist only of linear combinations of the parameters α_m and γ_{mn} and such combinations can be calculated very simply.

These characteristics of the matrix $H_{\mu\nu}$ make it possible to reduce the problem of full configuration interaction for a system of N electrons (with $N > K$) to the simpler problem of total configurational interaction for a system of $2K-N$ particles (holes). In this change from electrons to holes the off-diagonal $H_{\mu\nu}$ are not altered and the new $H_{\mu\mu}$ are calculated according to the same simple rules. For example, the full configuration interaction for thiourea $CS(NH_2)_2$ constitutes a two-electron problem involving a basis set of four molecular orbitals, while the PPP method constitutes a six-electron problem with the same basis set (two π electrons are contributed by each N atom and the C and S atoms each contribute one π electron).

The results of calculations on ethylene, the allyl radical and radical-ions, butadiene, and benzene with full configuration interaction have been compared with the experimental values and the results of calculations by the PPP method [84]. It was found that (1) the correlation energy E_{corr} (i.e. the difference between the energy of the ground state found with full configuration interaction and the energy of the ground state found by the PPP method) is given approximately by the relation

$$E_{corr.} \approx -(0.11 \div 0.13)\cdot N(\text{eV})$$

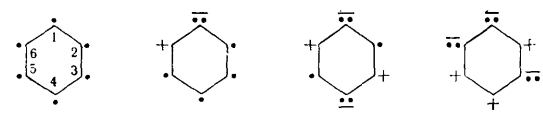
(this relation holds also for the benzyl radical [40]); (2) the optimum values of the parameters of the model Hamiltonian in the PPP method and in the method with full configuration interaction differ appreciably (Table 6). This confirms the view that the disadvantages of the approximate method are transferred to the effective parameters and the latter are therefore different for different methods.

Table 6. The excitation energies of benzene (PPP and full configuration interaction methods) [84] (eV).

Parameters	Method	Designation of energy state				
		$^1A_{1g}$	$^3B_{1u}$	$^1B_{2u}$	$^1B_{1u}$	$^1E_{1u}$
I	PPP	0 (−12.85)	3.7	4.8	5.9	6.75
	full CI	0 (−13.64)	3.35	4.1	6.2	5.07
II	PPP	0 (−15.5)	4.36	5.43	5.57	6.87
	full CI	0 (−16.17)	4.1	4.83	5.8	6.7
Experiment		—	3.7	4.8	5.9	6.76

I $\beta = -2.4$ $\gamma_{11} = 6.1$ $\gamma_{12} = 2.1$ $\gamma_{13} = 0.7$ $\gamma_{14} = 0$
II $\beta = -2.6$ $\gamma_{11} = 4.64$ $\gamma_{12} = 1.39$ $\gamma_{13} = \gamma_{14} = 0$

The covalent-ionic structure of the wave functions of benzene has also been studied [75,83,84]. Components with the coefficients $c_i(n_1 n_2 \ldots n_6)$, in which all the indices n_m are different, correspond to covalent structures in the function Φ; for unipolar structures, the coefficients have a single pair of identical indices (for example, $n_1 = n_2$); for dipolar structures, there are two pairs of indices ($n_2 = n_5$, $n_3 = n_6$), etc. Benzene structures with different polarities (with an indication of the atomic charges) are quoted below as an example:



The dots in the formulae denote π electrons. Non-zero coefficients of the type $c(123\,456)$, $c(112\,345)$, $c(124\,541)$, and $c(131\,366)$ correspond to these structures.

Table 7. Relative contributions (%) of covalent and polar (ionic) structures to the wave functions of certain benzene energy states [75,84].

Energy state, method of calculation		Type of structure			
		covalent	unipolar	dipolar	tripolar
$^1A_{1g}$	full CI	14.7	48.6	32.6	4.1
$^1A_{1g}$	Hückel method	7.9	42.7	42.4	7
$^3B_{1u}$	full CI	31.6	51.7	16.7	—

It was found that the polar structures make the main contribution to the ground state of benzene (see Table 7).

The contribution of each part of the function to the energy is approximately the same. Indeed calculation of

the energy of the ground state of benzene without vibrational structures (with polar structures alone!) increased the energy of the ground state (bond energy −16.17 eV) by only 2.3 eV. It is interesting to note that the contribution of covalent structures to certain excited states can increase [$^3B_{1u}$, the lowest benzene triplet (Table 7)] or can be rigorously equal to zero (for the $^1B_{1u}$ and $^1E_{1u}$ energy states of benzene).

Thus we conclude that structures of different polarity play different roles in the formation of different energy states. If we begin with the approximation in which structures of some kind are neglected, we shall be making different errors for different energy states. The non-uniformity of the contributions of different types of structures to different energy states and different properties can be used in calculations to reject insignificant structures.

These conclusions concerning the structure of the wave function demonstrate the lack of validity of the valence bond methods in which the role of covalent structures is overestimated.

The large contribution of polar (ionic) structures to wave functions is a consequence of the relative weakness of the Coulomb repulsion of π electrons in conjugated systems. In this connection it is interesting to note that, in the calculation on the ground state of benzene by the Hückel method (all the $\gamma_{mn} = 0$), the covalent-ionic structure of the wave function is reproduced correctly (Table 7). This is also a consequence of the relative weakness of the Coulomb interaction of π electrons and at the same time throws light on the relative success of the Hückel method in the calculation of certain properties of conjugated molecules and radicals.

d. The Hückel Method

Despite the development of various methods for calculations on conjugated systems, the simple Hückel molecular orbital method still retains its value and is frequently used. The Hückel method yields results which agree adequately with experimental data. This applies both to the properties of the ground state (bond lengths, charge densities, and spin densities) and to singlet excitation energies[9,85], ionisation potentials and electron affinities[86], and other properties of conjugated molecules[87]. The results of calculations on a large number of conjugated hydrocarbons by the Hückel method (molecular orbital coefficients and energies, bond orders, polarisabilities, etc.) have been tabulated[88,89]. Using these data for hydrocarbons the special perturbation theory of Coulson and Longuet-Higgins[88,89] greatly simplifies calculations, on the analogous molecules with heteroatoms.

Various versions of the Hückel method have been examined and analysed by Peacock[87]. Among other problems, he considered certain possibilities of improving the Hückel method based on known relations between Coulomb (α_n) and resonance (β_{mn}) integrals of the Hückel method on the one hand and the parameters of the effective PPP Hamiltonian on the other. The Hückel and PPP methods were compared in relation to a number of examples with analysis of the differences between the predictions of various molecular properties[86,87,90]. In particular, the inductive effect of π electrons can also be incorporated in the Hückel method using the so called ω technique (see, for example, Ehrenson[86]). This technique is analogous to the method whereby the inductive effect of electrons is taken into account in Scheme 2 of the PPP method (see the previous review[1]).

The Hückel method is also used to simplify calculations by the PPP method. One then employs the fact that self-consistent molecular orbitals are close to the molecular orbitals of the Hückel method. This makes it possible to use the Hückel molecular orbital method with the formal procedures of the PPP method to construct the excited configurations with subsequent determination of the excitation energies, etc. by the PPP method. Such a computational method has been used both for hydrocarbons[13] and for heterocycles[90].

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In conclusion we must mention that by no means all problems of the theory of conjugated systems have been considered here and in the previous review[1]. We may mention, for example, the theory of large conjugated systems, the theory of the reactivities of conjugated systems, and other problems which are important for the interpretation of experiments.

Examination of the vast quantum-chemical field which constitutes the semiempirical theory of conjugated systems is very difficult if only because the relevant research itself has not been completed. Therefore, in writing this review the authors frequently wished to postpone it and to undertake the development or simply the confirmation of certain aspects of the theory. If similar thoughts have also occurred to the reader, we can regard our task as fulfilled.

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Conformational Analysis of Bicyclo[3,3,1]nonanes

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The development of the principle of conformational analysis is associated mainly with the employment of cyclohexane and its heteroanalogues as model compounds. The present review surveys data on the conformational analysis of another system containing six-membered rings—bicyclo[3,3,1] nonane. A set of conformational problems, which have been successfully solved using the above bicyclic system, are discussed, the fundamental principles are formulated, and the great scope of the applications of this model in conformational research is demonstrated.
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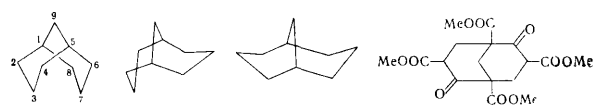
I. INTRODUCTION

The concepts of conformational analysis constitute an extremely effective tool in the hands of the chemist whereby it is possible to understand more deeply the mechanisms of a wide variety of processes. Hence there is clearly an urgent need for a deeper understanding of the concepts and theories of dynamic stereochemistry. The general postulates of conformational analysis are based to a large extent on data for cyclohexane derivatives, its polycyclic derivatives, and its heteroanalogues such as, for example, monosaccharide derivatives, six-membered heterocycles, etc. Nevertheless the employment of cyclohexane derivatives is not always most useful. For example, one of the fundamental problems involves the study of factors which determine the possibility of the existence and the energy of flexible forms (boat, "twist-form"); problems of the reactivity of the functional groups in these conformations are also fundamental. However, there are no convenient model compounds of the cyclohexane series with the boat conformation and with a sufficiently large set of functional groups suitable for the investigation of problems of this kind. Indeed the majority of compounds of this type assume the form of a somewhat deformed (usually flattened[1]) chair and the difference between the free energies of the boat and chair forms is fairly large (5—7 kcal mole^{-1}).[2,3] Therefore many approaches to this problem are associated with the synthesis of cyclic structures (frequently containing heteroatoms), which might exist in a flexible conformation or contain individual fragments which might simulate the geometrical relations in the flexible conformation of cyclohexane (see, for example, Whitlock[4] and Adachi et al.[5]).

The study of derivatives of bicyclo[3,3,1]nonane is of great interest in this connection. We emphasise that at the beginning of the present century Rabe et al.[6] already used the bicyclo[3,3,1]nonane system for the solution of certain problems in theoretical chemistry.

Three conformations free from angular strain can be postulated for bicyclo[3,3,1]nonane itself: dichair (I), chair-boat (II), and diboat (III). In 1922 Meerwein and Schürmann[7] proposed on the basis of intuitive considerations the double chair conformation for the so called "Meerwein's ester" (IV).



(I) (II) (III) (IV)

However, systematic studies on this conformational problem began little more than ten years ago and significant progress was achieved literally in the last few years. The bibliography on this question has been steadily expanding and considerable advances have now been achieved in the understanding of the general problems of the conformational analysis of bicyclononanes. In the present review an attempt is made to examine the present state of the subject, to formulate the fundamental conformational problems which might be solved by resorting to model bicyclononane systems, and to assess the prospects of research in this field. The data are treated on a logical and not a historical basis. Apart from a greater theoretical rigour, this is justified by the considerable development of this field in recent times, which makes it difficult and sometimes simply impossible to follow the historical genesis of the ideas and the questions of priority.

II. GENERAL PROBLEMS OF THE CONFORMATIONAL ANALYSIS OF BICYCLO]3,3,1]NONANES

Although conformations (I)—(III) are free from angular strain, nevertheless none is free from a strong destabilising interaction between the non-bonded atoms. The destabilisation of the boat conformations (II) and (III) is due to the same factors which operate in the case of the boat conformation of cyclohexane, namely the presence of eclipsed ethane conformations and the flagpole—flagpole repulsion between the hydrogen atoms[2]. In the chair-boat

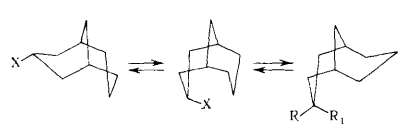
structure (II) the ring in the boat form cannot be appreciably deformed to give the twist-form owing to the rigidity of its junction with the second ring. One can probably imagine only a moderate twisting. However, since for each chair-chair conformation (I) one obtains in the inversion process two chair-boat conformations (II), the latter conformation is twice as likely to be produced. In other words the formation of form (II) is preferred on entropy grounds to the extent of $R \ln 2$. On the other hand, the diboat conformation (III) should correspond to the maximum on the energy curve. A twisted conformation, which can be called the ditwist-form, corresponds to the minimum. In this conformation the flagpole and eclipsed interactions, which are characteristic of the undistorted form (III), are appreciably diminished. This conformation is the only flexible form and is therefore more favourable from the standpoint of the entropy factor.

The chair conformation is usually greatly stabilised by the enthalpy factor (see, for example, Zefirov and Kazimirchik[8]). However there is a specific destabilising factor for the dichair conformation (I), namely the extremely powerful attraction of the *endo*-hydrogen atoms in the 3- and 7-positions. Simple calculations using the normal angles and bond lengths show that the difference between the 3-*endo*- and 7-*endo*-hydrogen atoms should be only 0.81 Å![3] We may recall that the van der Waals radius of hydrogen is 1.2 Å.[9] Therefore in the initial studies the authors gave preference to the chair-boat conformation (II) (for example in the investigations of de la Mare et al.[10] and Leonard and Morrow[11]; however, see Hall[12]) and this view has been reflected in textbooks[13].

However, one must emphasise that the above structures are limiting and one can imagine that in specific instances these ideal forms will suffer greater or smaller distortions, which will lead to a decrease of strain. For example, the flattening of the six-membered rings in conformation (I) and the bending of the C—H bonds in the 3- and 7-positions (i.e. the decrease of the $H-C_{(3)}-H$ or $H-C_{(7)}-H$ angle) can reduce the internal energy. Below it will be shown that such changes in geometry do indeed occur, as a result of which the double chair conformation is usually the most stable.

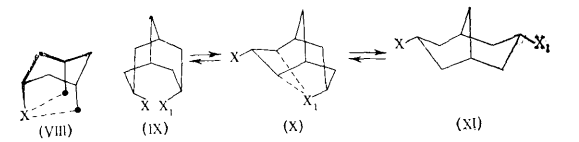
Furthermore, one can determine fairly reliably certain conformational trends arising on passing to functional derivatives and associated with the introduction of substituents, heteroatoms, etc.

Firstly, it is quite evident that the introduction of a 3-*endo*- or 7-*endo*-substituent more bulky than the hydrogen atom will cause a sharp increase of the steric repulsion in the dichair conformation (V) and its sharp destabilisation. Of the two alternative chair-boat conformations, (VI) and (VII), conformation (VI), which has a substituent in the bowsprit position [which is approximately equivalent to the position of the substituent in the equatorial conformation (VIIa)], should be more stable.



(VI) (V) (VII, R = H, R_1 = X; VIIa, R = X, R_1 = H)

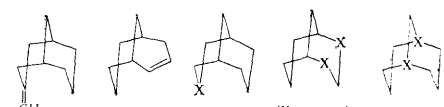
Secondly, the 3-*endo*- and 7-*endo*-positions in conformation (I) are equivalent to the axial position for cyclohexane derivatives of type (VIII). Therefore a functional derivative of type (V) or (VII) is subjected to two additional 1,3-axial interactions, analogous to those in (VIII).



(VIII) (IX) (X) (XI)

Although the extent of such interaction should be different from that observed in cyclohexane by virtue of the differences in geometry, nevertheless one can imagine that in the presence of a very bulky group X in compound (V) such interaction should lead to the destabilisation of the dichair form. For a monofunctional derivative of type (V), this factor is indistinguishable from the previous factor associated with the 3—7 repulsion factor [it will evidently effect the relative stabilities of forms (VI) and (VII), hindering strongly conformation (VI)]. However, in 3—7 disubstituted derivatives (IX) this factor can stabilise the diboat conformation (XI), but not the chair-boat conformation (X).

Thirdly, it is possible to trace certain tendencies associated with the introduction of trigonal carbon atoms into the bicyclononane skeleton. Thus it is evident that the introduction of a trigonal atom in the 9-position should lead to some stabilisation of the boat conformations (II) and (III) owing to the elimination of the flagpole—flagpole interaction, although it is difficult to predict *a priori* the extent of such stabilisation. Furthermore, the introduction of a trigonal atom in the 3-position, for example in compound (XII), leads to a decrease of the 3—7 repulsion and hence to the stabilisation of the dichair form. The introduction of a double bond in the 2,3-positions, as in compound (XIII), should also result in a marked flattening of the cyclohexene ring and a sharp diminution of the 3—7 repulsion.



(XII) (XIII) (XIV) (XV, X = O; XVII, X = S) (XVI)

In conclusion of this section one should note particularly that many problems in the conformational analysis of bicyclo[3,3,1]nonanes have been studied in relation to heteroanalogues of this system. In broad outline, the geometry of bicyclic molecules containing the "usual" heteroatoms (oxygen, nitrogen, and even sulphur) simulates fairly satisfactorily the geometry of the carbon analogue. For example, it is not fortuitous that the conformational analysis of six-membered heterocycles reveals in broad outline the same fundamental conformational characteristics as were discovered for cyclohexane derivatives[8,14,15]. Therefore in this case one can preduct beforehand certain conformational features. Thus the introduction of a heteroatom in the 3-position, as in compound (XIV), should lead to the stabilisation of the dichair conformation by virtue of the decrease of the 3—7 repulsion. Furthermore, the introduction of heteroatoms into the bicyclononane skeleton leads to changes in the geometry which largely depend on the relative lengths of the C—C and C—heteroatom bonds. If the latter is appreciably shorter, the introduction of heteroatoms in the 2- and 4-positions, as in compound (XV), or in the 1- and 5-positions, as in compound (XVI), should lead to an enhancement of the 3—7 repulsion. The converse should also

probably be true, namely a decrease of the 3—7 repulsion with increase in the length of the C—heteroatom bond, as in compound (XVII).

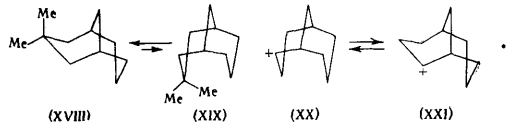
However, many "anomalies", "effects" specific to heterocyclic compounds, due to the electrostatic interactions of the heteroatoms, the interactions of the lone electron pairs, etc. are now known[8,9,16-27]. Therefore it is necessary to examine critically data on the heteroanalogues, bearing in mind the specific features of the model compounds investigated. On the other hand, the use of heteroanalogues significantly extends the range of problems which can be solved with the aid of the bicyclic model.

III. CALCULATIONS OF THE GEOMETRY AND ENERGY

To calculate the geometry and relative energy of molecules, either semiempirical quantum-chemical methods or Westheimer's classical approach are used nowadays[28,29]. The latter is widely employed in its current modifications for the calculation of the geometries of fairly complex compounds[3,30-36]. The first calculation on the bicyclo[3,3,1]nonane molecule by this method was carried out by Gleicher and von R. Schleyer[37], who calculated the geometry for the dichair conformation only. The $C_{(3)}\ldots C_{(7)}$ distance was estimated as 2.96 Å (cf. 2.56 Å for the ideal form[3,38]) and the $C_{(1)}C_{(2)}C_{(3)}$ angle was estimated as 113°. These data indicate a considerable flattening of the "wings" of the molecule. A more rigorous calculation was performed by Allinger and coworkers[3,38]. In this case too the dichair conformation differed fairly appreciably from the ideal conformation. In the first place the $C_{(3)}\ldots C_{(7)}$ distance increased to 3.18 Å and the $H_{(3)}C_{(3)}H_{(3)}$ and $H_{(7)}C_{(7)}H_{(7)}$ angles decreased to 95.2°. This resulted in an increase of the *endo*-$H_{(3)}\ldots$*endo*-$H_{(7)}$ distance from 0.81 Å for the ideal structure to 2.25 Å. Nevertheless, despite the considerable distortion of the structure and the strong non-bonding interaction, the dichair conformation (I) is more stable than the chair-boat conformation (II). Calculation of the enthalpy difference yielded 2.73 kcal mole^{-1} in favour of conformation (I).[3,38] Another calculation gave 3.7 kcal mole^{-1} for this difference[39]. However, the authors point out that this value may be too high.

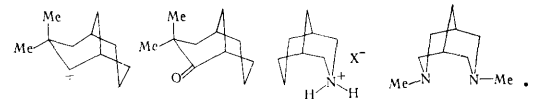
In another instance the calculated ΔH was appreciably less than 5.9 kcal mole^{-1} adopted for the enthalpy difference between the flexible and chair forms of cyclohexane[2,8,40]. Evidently this difference is caused by the appreciable relative destabilisation of the dichair.

The situation for 3,3-dimethylbicyclo[3,3,1]nonane differs significantly. A calculation has shown[39] that conformation (XVIII) is more stable to the extent of 3.9 kcal mole^{-1} than (XIX):



(XVIII) (XIX) (XX) (XXI)

The geometries of certain carbenium ions, incorporated in the bicyclo[3,3,1]nonane skeleton, have also been calculated by this method[37,39]. Thus it has been found that the dichair conformation (XX) of the 2-bicyclo[3,3,1]nonyl cation is more stable than conformation (XXI) to the extent of 2.7 kcal mole^{-1}.[39] The chair-boat conformation of the cation (XXII) is more stable than the dichair conformation, the difference between the energies being 4.4 kcal mole^{-1}.[39] Data for the carbonium ions are not only of intrinsic interest but also as model data for compounds with a trigonal carbon atom; for example, the above calculation confirms the greater stability of the chair-boat conformation of the ketone (XXIII):[39]

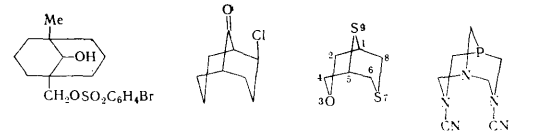


(XXII) (XXIII) [XXIV, (a) X = Br; (b) X = Cl] (XXV)

Semi-empirical quantum-chemical methods—the extended Hückel and CNDO/2 methods—have been used in calculations on the conformations of the aza-analogues of bicyclo[3,3,1]nonane[41]. Thus the hydrobromide (XXIVa) has an energy minimum in the dichair conformation with a $C_{(7)}\ldots N_{(3)}$ distance of 2.9 Å. Dimethylbispidine (XXV) also has a minimum for the dichair conformation, but the $N_{(3)}\ldots N_{(7)}$ distance is 2.5 Å, which is close to the corresponding distance in the ideal conformation. Evidently the main difference is associated with the presence of the 3- and 7-*endo*-hydrogen atoms in compound (XXIV). We may also note that the problem of the conformations of the 3,7-diheteroanalogues is of special interest in connection with the problem of the dipole—dipole or orbital interaction between the heteroatoms (see Section VI, 5).

IV. EXPERIMENTAL DATA ON THE GEOMETRY OF BICYCLO[3,3,1]NONANE DERIVATIVES

The first X-ray diffraction studies showed that the double chair conformation is characteristic of the majority of carbocyclic and heterocyclic bicyclo[3,3,1]nonane derivatives. Dobler and Dunitz[42] were the first to show that the hydrobromide (XXIVa) of 3-azabicyclononane has a flattened dichair conformation. The $N_{(3)}\ldots C_{(7)}$ distance is increased to 3.02 Å owing to the flattening (see the calculation of Chakrabarty et al.[41]). The $H_{(3)}\ldots H_{(7)}$ distance between the *endo*-hydrogen atoms can be estimated as 1.8 Å.[43,44] The molecular structure of a carbocyclic compound—the *p*-bromobenzenesulphonate (XXVI)—has been determined[43,44]. Both rings in (XXVI) have a distinct chair conformation, but the structure deviates appreciably from ideality and the two rings are appreciably flattened.



(XXVI) (XXVII) (XXVIII) (XXIX)

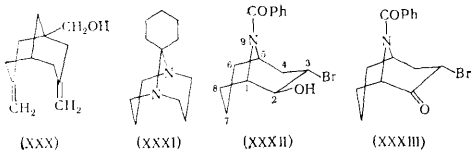
The $C_{(2)}C_{(3)}C_{(4)}$ and $C_{(6)}C_{(7)}C_{(8)}$ angles are on average 114° and the $C_{(3)}\ldots C_{(7)}$ distance is 3.05 Å. The structure of the chloroketone (XXVII) has been determined[45]. The steric repulsion of the methylene groups also leads to the flattening of the molecule and the $C_{(3)}\ldots C_{(7)}$ distance is 3.11 Å, which is much more than 2.1 Å expected for the ideal bicyclononon-9-one. We must emphasise that neither the presence of a trigonal atom in the 9-position nor the presence of the 2-*exo*-substitute in the ketone (XXVII) leads to the destabilisation of the dichair conformation. We may also recall the data concerning

the structure of the 3,7-diheteroanalogues of bicyclononane. It has been found[46,47] that 3-oxa-7,9-dithiabicyclo[3,3,1]nonane (XXVIII) exists in the dichair conformation. It is interesting that the plane passing through the $C_{(1)}$, $S_{(9)}$, and $C_{(5)}$ atoms intersects the $C_{(2)}O_{(3)}C_{(4)}$ plane at an angle of 2° and the $C_{(6)}S_{(7)}C_{(8)}$ plane at an angle of 32°45′. The appreciable flattening of the dithiane ring is evidently associated with the smaller barrier to rotation about the C—S bond compared with the C—O bond (see the relevant discussion in the author's earlier review[8]). A dichair conformation was also found for compound (XXIX), the angles $N_{(1)}C_{(2)}N_{(3)}$ and $N_{(1)}C_{(8)}N_{(7)}$ being 133—136°.[48]

There are literature data for the geometry of bicyclo[3,3,1]nonane itself[49]. It too has the dichair conformation, since it forms mixed crystals with adamantane in which this "conformation" is rigidly fixed. The lattice parameters led to the conclusion that the molecule is flattened; unfortunately the parameters of the molecular structure were not determined (for other X-ray diffraction data, see Sections VI, 5 and VI, 6).

Thus X-ray diffraction results have shown that in the crystal the dichair conformation is preferred, with an appreciable flattening of the wings of the molecule, which leads to an increase of the valence angles in the 2-, 3-, 4-, 6-, 7-, and 8-positions by 4° relative to the normal value.

There are certain data on the geometry of compounds of the above type in solution. Thus the identity of the infrared spectra in solution and in the solid phase for compounds (XXVI) and (XXVII) [43,44,50] makes it possible to extend the X-ray diffraction data also to the geometry of the molecule in solution. The development of studies on molecular geometry in solution is associated mainly with two modifications of the NMR method. Firstly, this involves the use of shift reagents[51,52]. Thus a study has been made[53] on the chemical shifts induced in the presence of Eu(DPM)$_3$ † for 1-hydroxymethyl-3,7-dimethylenebicyclo[3,3,1]nonane (XXX).



(XXX) (XXXI) (XXXII) (XXXIII)

The $C_{(3)}\cdots C_{(7)}$ distance was estimated as 3.1 Å, in agreement with the dichair structure (for the limitations of the method, see Section VI, 6).

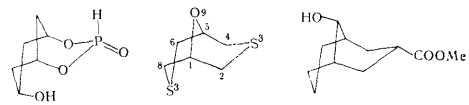
Secondly, a convenient means of investigating the geometry of six-membered systems is provided by the so called NMR "*R*-method".[54-57] In particular, this method has been used to investigate 1,5-diazabicyclo[3,3,1]nonane (XVI, X = N) and its pentamethylene derivative (XXXI).[53] The spin—spin coupling constants for the fragment $-CH_2-CH_2-$ in these compounds indicate an appreciable flattening, which leads to a decrease of the $N_{(1)}C_{(2)}C_{(3)}C_{(4)}$ dihedral angle to 48° and 45° respectively (cf. the 54.5° angle for cyclohexane[1]). This is satisfactorily correlated with the X-ray diffraction studies: the analogous dihedral angles of compounds (XXVI) are in the range 43.6—45.2°;[44-58] in compound (XXIVa) the dihedral angles are 43.0° in the cyclohexane ring and 50.2° in the piperidine ring[42,58].

†DPM = dipivaloylmethane.

As shown in Section II, the appearance of the boat conformations (II) and (III) may be expected when there is a sharp enhancement of the non-bonding interactions, which usually takes place after the introduction of bulky substituents in the 3-*endo*-position. The first compound investigated in this series was 9-benzoyl-3-*endo*-bromo-2-*exo*-hydroxy-9-azabicyclo[3,3,1]nonane (XXXII).[59,60]

As was to be expected, the substituted ring assumes the boat form. The amide nitrogen atom $N_{(9)}$ is planar, so that the geometry of the molecule of (XXXII) resembles that of bicyclo[3,3,1]nonan-9-one [for example, compound (XXVII)]. The $C_{(3)}\cdots N_{(9)}$ distance is 2.56 Å. The displacements of the $C_{(3)}$ and $C_{(7)}$ atoms from the $C_{(1)}C_{(2)}C_{(4)}C_{(5)}$ and $C_{(5)}C_{(6)}C_{(8)}C_{(1)}$ planes are respectively 0.64 and −0.63 Å, which is more than in the dichair conformation [0.51 Å for the ketone (XXVII) [45]], but less than for the ideal cyclohexane conformation (0.73 Å). Thus the ring having the chair form in the chair-boat conformation is distorted much less than in the dichair conformation. These data were confirmed by a study of the structure of the ketone (XXXIII).[61] The molecule of (XXXIII) also assumes the chair-boat conformation with a $C_{(3)}\cdots N_{(9)}$ distance of 2.61 Å and with displacements of the $C_{(3)}$ and $C_{(7)}$ atoms from the $C_{(1)}C_{(2)}C_{(4)}C_{(5)}$ and $C_{(5)}C_{(6)}C_{(8)}C_{(1)}$ planes of 0.64 and −0.65 Å.

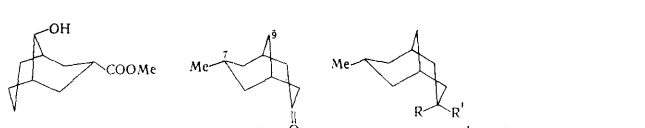
There are literature data for the boat conformations of the heteroanalogues of bicyclo[3,3,1]nonane. Thus it has been found[62,63] that one of the isomeric alcohols (XXXIV), obtained in the acid cleavage of phosphatrioxa-adamantane derivatives has the chair-boat conformation, the heterocyclic ring being in the boat form (see Section VI, 3).



(XXXIV) (XXXV) (XXXVI)

It has been shown[46,47] that 9-oxa-3,7-dithiabicyclo[3,3,1]nonane (XXXV) has the chair-boat configuration; the $C_{(2)}S_{(3)}C_{(4)}$ and $C_{(6)}S_{(7)}C_{(8)}$ planes intersect the $C_{(1)}C_{(5)}O_{(9)}$ plane at angles of 76°9′ and 11°45′ respectively. The $S_{(3)}\cdots O_{(9)}$ distance is 2.84 Å (for the relevant discussion and other data, see Section VI, 5).

Only isolated data are available for the geometry of conformation (II). The chair-boat conformation has been demonstrated[64] by the shift reagent method for the epimeric hydroxyesters (XXXVI) and (XXXVII), but the geometrical parameters were not determined (see also Vegar and Wells[65]).



(XXXVII) (XXXVIII) (XXXIX, R = OH, R′ = Me)

[XL, (a) R = OH, R′ = H; (b) R = H, R′ = OH]

A study of the induced chemical shifts established that compounds (XXXVIII), (XXXIX), and (XLa) have the chair-boat conformation with $C_{(7)}-C_{(9)}$ distances of 2.8, 2.65, and 2.65 Å respectively[66] (cf. Kimoto et al.[52]).

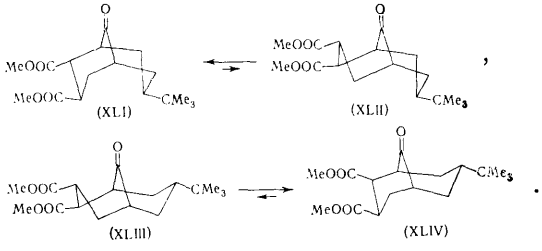
Thus X-ray diffraction data confirm the conclusion reached in Section II that the introduction of a 3-*endo*-substituent stabilises the chair-boat conformation. Despite the small number of experimental results, one may conclude that the geometry of the ring in the chair

form in this conformation is closer to that of the usual cyclohexane derivatives. The smallest intramolecular contact in conformation (II) obtains for the $C_{(3)}...C_{(9)}$ distance (or $C_{(7)}...C_{(9)}$ depending on the numbering system).

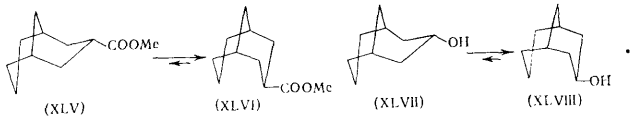
There are no literature data for conformation (III).

V. EXPERIMENTAL VALUES OF THE THERMODYNAMIC PARAMETERS OF THE CONFORMATIONAL EQUILIBRIA IN THE SYSTEM

As already mentioned in Sections II and III, one of the main problems in the conformational analysis of bicyclononanes is the determination of the relative stabilities of different conformations and the derivation of energy relations between them. Qualitative data can be obtained from results on the epimerisation of the corresponding functional derivatives. For example, the overall isomerisation of the methoxycarbonyl derivatives takes place on a preparative scale in the direction (XLII) → (XLI) and also (XLIII) → (XLIV).[67]‡ Bearing in mind the configurations of the compounds (see Sections VI, 3 and VI, 4) and hence the fact that epimerisation in controlled by the change in the conformation of the skeleton, these data make it possible to establish a qualitative sequence corresponding to the decrease of the energies of the conformations: diboat > chair-boat > dichair[67].



The first quantitative data were probably obtained in a study of the epimerisation of the esters (XLV) and (XLVI).[68] The equilibrium position was achieved starting from both isomers and the observed equilibrium constant corresponds to $\Delta G_{20^\circ} = -2.7$ kcal mole^{-1}. On the basis of the foregoing (see Sections II and IV), this value was assumed to be the difference between the free energies of conformations (I) and (II).

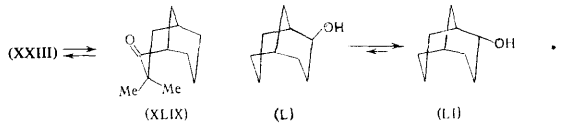


The analogous epimerisation of the isomeric alcohols (XLVII) and (XLVIII) gives rise to an equilibrium mixture containing 96.4% of the *exo*-isomer (XLVIII). Hence $\Delta G_{94^\circ} = -2.51$ kcal mole^{-1}.[69] This value is satisfactorily correlated with that observed by Appleton et al.[68] Since ΔG is independent of the nature of the substituent, this shows clearly that the difference between the free energies can be attributed solely to the different conformations of the skeleton.

‡ The paper of McEuen et al.[67] should also be referred to for the definitions of the terms adopted in the present review to designate different positions (bowsprit, gunnel, etc.).

If it is assumed that the entropies of the two conformers are the same§, then ΔH is 2.5–2.7 kcal mole^{-1} and can be compared with the energy difference calculated theoretically (see Section III). It is readily seen that the agreement between the experimental and calculated values is fairly satisfactory.

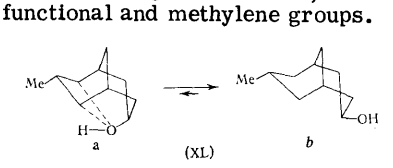
It has been found[39] that the ^{1}H NMR spectrum of the ketone (XLIX) depends on temperature. If it is assumed that this is related to the conformational equilibrium, ΔH can be estimated as 1 kcal mole^{-1}. The authors believe that this is also associated with an equilibrium of the type (I) ⇌ (II) and postulate a greater stability of conformation (XXIII) (see Section VI, 2).



There are no quantitative data on the conformational equilibrium (II) ⇌ (III).

There are also isolated literature values of ΔG_R for the substituents in the bicyclononane fragment. Thus epimerisation of bicyclo[3,3,1]nonan-2-ols (L) and (LI) yields values of ΔG_{OH} equal to −0.56 kcal mole^{-1} [69] and −0.559 kcal mole^{-1} [70] in isopropyl alcohol and −0.25 kcal mole^{-1} [69] in cyclohexane. It is interesting to compare these values with those found for cyclohexanol: 0.52 kcal mole^{-1} in aprotic media and 0.87 kcal mole^{-1} in protic solvents[71]. The equilibrium epimerisation of 2-methylbicyclo[3,3,1]nonanes at 230°C leads similarly to a mixture containing 72% of the equatorial isomer[72]. Hence it is possible to estimate $\Delta G^{230^\circ C}_{Me}$ as approximately 1 kcal mole^{-1}. This value is also much lower than that observed for methylcyclohexane (1.70 kcal mole^{-1}).[71] The decrease of ΔG_R for the 2-position in the bicyclo[3,3,1]nonane system can be attributed to the occurrence of the equatorial *endo*-$R_2...$*endo*-$H_{(8)}$ interaction[39,69].

Interesting data on the epimerisation of the alcohols (XL, a and b) have been obtained[52]. The authors found that the free energy difference $\Delta G_{OH} = -2.18$ kcal mole^{-1} when equilibrium is established in isopropyl alcohol at 110°C. Evidently this difference cannot be attributed to an equilibrium of the type (I) ⇌ (II), but in fact represents the conformational energy of the substituent (cf. Hirsch[71]). The difference between the conformational energies must therefore be due to the occurrence of two unfavourable 1,3-axial–axial $CH_2...OH$ interactions in conformation (XLa) compared with the analogous $CH_2...H$ interactions in conformation (XLb). Assuming that the energy of the first is 1.9 kcal mole^{-1} [2] and that of the second −0.85 kcal mole^{-1},[2,71] it is possible to estimate the difference between the conformational energies as 2.1 kcal mole^{-1}. This agrees very well with the experimental value. It is also evident that the bicyclo[3,3,1]nonane system may be convenient for the investigation of the 1,3-interaction between the functional and methylene groups.

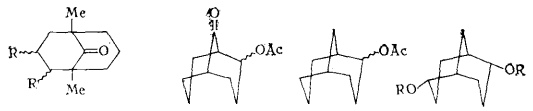


§ This hypothesis implies the neglect of the contribution of the alternative chair-boat conformation and hence of the entropy of mixing $R(x_1 \ln x_1 + x_2 \ln x_2)$.

VI. CONFORMATIONS OF FUNCTIONAL DERIVATIVES AND HETEROANALOGUES OF BICYCLO[3,3,1]NONANE

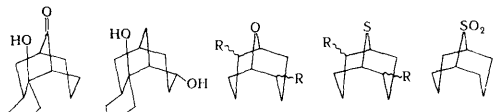
1. Determination of the Conformations of Bicyclo-[3,3,1]nonanes by Infrared Spectroscopy and ^{1}H NMR

The characteristic features of the application of infrared spectroscopy for a qualitative assignment of the conformations in the bicyclo[3,3,1]nonane series are based on the following factor. The spectra of polycyclic and skeletal compounds, in which two or more methylene groups are sterically in very close proximity, are known to contain anomalous infrared absorption bands due to C—H bonds in the region of 1490 and 2990 cm^{-1}. The infrared spectra of many bicyclo[3,3,1]nonane derivatives also contain these bands, which has been attributed to the $C_{(3)}H_2 \ldots C_{(7)}H_2$ interaction in the double chair conformation[43,44,73,74]. The proof is based on the following data[43,73]. Compound (LIIa) has an absorption band at 1490 cm^{-1}, whence it follows that the possible $C_{(3)}—C_{(9)}$ or $C_{(7)}—C_{(9)}$ interactions are not the cause of this anomaly. The intensity of this band in the infrared spectrum of the deuteriated compound (LIIb) is approximately halved. We may note that in the adamantane infrared spectrum there is no absorption in this region[75].



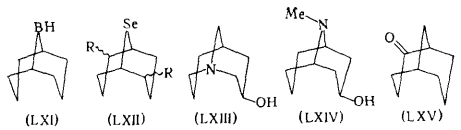
[LII, (a) R = H; (b) R = D] (LIII) (LIV) (LV, R = MeCO; LVa, R = H)

The high-frequency stretching vibration band at 2990 cm^{-1} and the deformation vibration band at 1490 cm^{-1} indicate the existence of the dichair conformation. The conformations of the ketone (XXVII) and its equatorial epimer[50], of the acetates (LIII),[76] (LIV),[77] and (LV),[78] of the alcohol (XLVIII)[69] and its 1,5-dimethyl analogue[79], of the condensed systems (LVI) and (LVII),[80] etc. were elucidated in this way. We emphasise that the dichair conformation of many 9-heteroanalogues of the bicyclo-[3,3,1]nonane system, for example of compounds (LVIII),[81-83] (LIX),[84,85] (LX),[85] (LXI),[86] and (LXII),[87] was in fact demonstrated by infrared spectroscopy.



(LVI) (LVII) R = Br, I, OAc, HgX (LVIII) R = H, Cl (LIX) (LX)

Infrared spectroscopy makes it possible to distinguish reliably bicyclo[3,3,1]nonane derivatives from the isomeric bicyclo[4,2,1]nonane derivatives[77,82,83,85,87], which are frequently obtained as a mixture in syntheses bases on cyclo-octadiene[88].

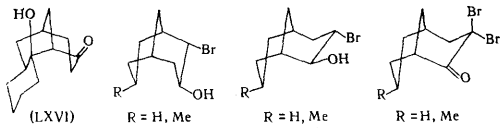


(LXI) (LXII) (LXIII) (LXIV) (LXV)

However, in many cases it was noted that the above absorption bands are not shown in the infrared spectrum even if the compound is known to exist in the double chair conformation. As an example, we may mention the aminoalcohols (LXIII) and (LXIV).[89] These bands are absent from the infrared spectra of the ketones (LXV)[77] and (LXVI).[80] In the latter case the presence of the trigonal carbon atom is responsible for the more planar ring conformation and hence for the significant separation of the transannular methylene groups (see Section VI, 2).

The application of ^{1}H NMR in this series of compounds is based on the familiar characteristics of the changes in the chemical shifts of the *a*- and *e*-protons and, what is more important, on the relation between the constant $^3J_{HH}$ and the dihedral angle (the Karplus equation). In conformation (I), the vicinal constants for the $H_{(1)}H_{(2)}$ and $H_{(2e)}H_{(3)}$ protons correspond to the *ae*- or *ee*-constant (2—4 Hz) and the constants of the $H_{(2a)}H_{(3a)}$ protons correspond to the *aa*-constant (9—12 Hz) for cyclohexane derivatives. Two larger $H_{(1)}H_{(2e)}$ (approximately 10 Hz) and $H_{(2a)}H_{(3)}$ (approximately 10—12 Hz) proton coupling constants should be observed for the boat conformation. The greatest difficulty is associated with the following factor: in conformational analysis there exist two alternative chair-boat conformations, as a result of which there is no sharp change in the hyperfine coupling constants. Furthermore, the flattening of the wings of the molecule in conformation (I) also increases the constant $J_{H_{(1)}H_{(2a)}}$ (for a detailed discussion of this problem, see Zefirov and Rogovina[90]). For the monosubstituted derivatives of type (VI), (V), (L), (LI), (LIV), (LV), (LVIII), etc., a clear-cut assignment can be achieved when a large (in excess of 9 Hz) vicinal hyperfine coupling constant is observed. All these features have been widely used to elucidate the configurations of the substituents and also for conformational assignments[52,77,91-100].

In particular, the conformation of the alcohol (XLVIII)[69,99] and its 1,5-dimethyl analogue[79], of the epimeric alcohols (XL, a and b),[52,53] of the epimeric chloroketones of the type (XXVII),[50] of the isomeric bromohydrins (LXVII) and (LXVIII),[68] and of the dibromoketone (LXIX)[68] were demonstrated by ^{1}H NMR.

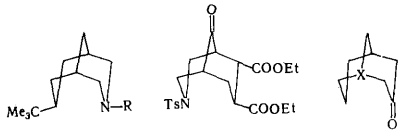


(LXVI) R = H, Me (LXVII) R = H, Me (LXVIII) R = H, Me (LXIX)

2. Conformations of Carbonyl Derivatives of Bicyclo-[3,3,1]nonane and its Monoheteroanalogues

In the first place it is necessary to consider the conformational analysis of monoheterobicyclo[3,3,1]nonanes. From the foregoing data, it is already clear that a wide variety of 2-*endo*-, 2-*exo*-, and 3-*endo*-monosubstituted derivatives of bicyclo[3,3,1]nonane and also 9-heterobicyclo[3,3,1]nonanes exist preferentially in the double chair conformation. The introduction of heteroatoms in the 1-, 2-, and 3-positions also should not apparently alter qualitatively the relative stabilities of the conformations. Although there are no data for 1-azabicyclo-[3,3,1]nonane, the existence of the 1,5-diaza-derivatives (XVI, X = N) and (XXXI) in the dichair conformation[58] confirms this view. There are literature data showing that 3-azabicyclononanes also exist in the dichair conformation for a wide variety of substituents at the nitrogen

atom. The amine (LXX),[93] *N*-benzoyl-3-azabicyclo-[3,3,1]nonane (XIV, X = $NCOC_6H_5$),[92] the toluene-*p*-sulphonate (LXXI),[101] and the hydriodide of *N*-methyl-3-azabicyclo[3,3,1]nonane[91] may be quoted as examples. It has been found by ^1H NMR that derivatives of 3-oxabicyclo-[3,3,1]nonane (XIV, X = 0) [102,103] and even of 3-thiabicyclo-[3,3,1]nonane (XIV, X = S) [90] exist in the dichair conformation. The latter example shows that even the introduction of a bulky hexoatom such as sulphur does not lead to qualitative changes in the relative energetic stabilities of conformations (I) and (II).

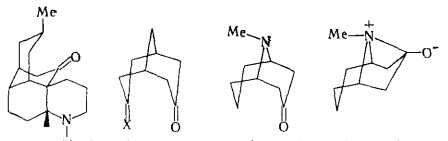


(LXX) (LXXI) (LXXII, X = CH) (LXXIII, X = N)

We shall now consider the problem of the conformational analysis of carbonyl compounds. The introduction of a carbonyl group in the six-membered ring is known to decrease appreciably the difference between the enthalpies of the boat and chair conformations; for example, the enthalpy of the boat–chair conformational transition of cyclohexanone is only 3.9 kcal $mole^{-1}$.[36,39,68] Therefore the introduction of the carbonyl group should decrease the difference between the energies of conformations (II) and (I). On the other hand, the introduction of a trigonal atom should cause some flattening and hence some stabilisation of form (I) as a result of the diminution of the 3–7 repulsion. When the C=O group is introduced into the 3-position, the repulsion of hydrogen atoms is altogether eliminated and only the *endo*-$H_{(7)} \ldots C_{(3)}$=O interaction remains. It is difficult to predict the balance of these factors, particularly for 2-oxo-derivatives[39,68].

The experimental data for 9-oxo-derivatives show that these compounds exist in the dichair conformation [compounds (XXVII),[45,50] (LII),[43,73] (LIII),[76] and (LVI) [80]]. This was to be expected, since the fragment with the carbonyl group is part of the rigid bridge system and a decrease in the barrier to rotation about the CO–C bond cannot affect the conformational energy. However, the data for 3-oxo-derivatives are contradictory. The conformation of bicyclo[3,3,1]nonan-3-one (LXXII) itself was investigated by ^1H NMR using a shift reagent[65]. It follows from the variation of the proton chemical shift with the concentration of the shift reagent that the carbonyl-containing ring must be planar. This was interpreted as indicating a conformational equilibrium between the dichair and chair-boat forms with a 1 : 1 conformer ratio. However, ultraviolet spectroscopic and ^1H NMR data for the 1-aza-analogue (LXXIII) indicate a pronounced flattening in the dichair conformation[104]. Detailed study of the conformation of the parent ketone (LXXII) should probably be continued.

We may note that X-ray diffraction analysis led to the determination of the geometry of the product obtained by the cleavage of the methiodide of lycopodine (LXXIV).[105] The bicyclononanone fragment is forced to adopt the dichair conformation, because the cyclohexane ring forms part of the rigid polycyclic system and the methyl group fixes the conformation of the second ring.

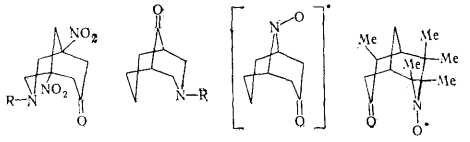


(LXXIV) [LXXV (a) X = CH_2; (b) X = O] (LXXVI) (LXXVII)

There are no data for the conformation of 3-methylenebicyclo[3,1,1]nonane (XII). Bearing in mind that 3,7-dimethylenebicyclononanes of type (XXX) exist in the dichair conformation[53], presumably the same conformation will be preferred also for ketones of type (LXXV).

In analysing the conformational equilibria of aminoketones, it is necessary to take into account an additional factor, namely the interaction of these groups in the direction $R_3\overset{+}{N} + C{=}O \rightarrow R_3\overset{+}{N}{-}C{-}O^-$. Transannular interactions of this type have been studied fairly thoroughly[106–109]. In the bicyclononane series this problem was encountered in a study of pseudopelletierine (LXXVI). The infrared spectrum of this compound indicates the absence of a transannular interaction between the amino- and carbonyl fragments of type (LXXVII), which supports the dichair conformation[108]. This was also confirmed by dipole moment data[108] and measurements of the Kerr constants[110]. The ^1H NMR spectra led to the conclusion that pseudopelletierine is in the conformation (LXXVI) with pronounced distortion of the piperidinone ring[98]. Possibly the marked flattening prevents the transannular interaction between the amino- and carbonyl groups in compounds of type (LXXVIII).[107] Similarly the aminoketone (LXXIX) also exists in the dichair conformation. The absence of an interaction between amino- and carbonyl fragments in the chair-boat conformation follows from dipole moment data and infrared spectra[111]. The infrared spectra do not contain bands in the range 2600–2800 cm^{-1}.[112,113]

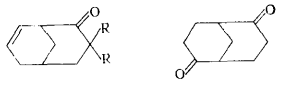
X-Ray diffraction analysis of the free radical (LXXX), which exists in a dimeric form, showed that it has the dichair conformation[114]. However, it is possible that the assumption of a tetracoordinate configuration by nitrogen on formation of the dimer is responsible for the destabilisation of the chair-boat conformation. Judging from the ESR spectrum and the dipole moment, another nitroxyradical (LXXXI) also exists in the dichair conformation[115].



(LXXVIII) (LXXIX) (LXXX) (LXXXI)

Only isolated data are available for 2-oxo-derivatives. There are no experimental results for the ketone (LXV), although (see Section III) a number of investigators tend to give preference to the chair-boat conformation on the basis of indirect evidence[39,68]. The equilibrium (XXIII) ⇌ (XLIX) has been observed for the 3,3-dimethyl-2-oxo-derivative (see Section V). However, the conformation of the more stable isomer has not been demonstrated experimentally[39]. As stated in Section II (see also Section VI, 7), the introduction of a double bond leads to a flattening of the ring, which tends to reduce the strain in conformation (I). Therefore the chair-half-chair conformation has been postulated for the ketone (LXXXIIa)[39].

The authors assume the same conformation also for the dimethyl derivative (LXXXIIb) on the basis of the similarity of its ultraviolet spectrum to that of the unsubstituted ketone, which naturally cannot be regarded as very reliable evidence.



[LXXXII, (a) R = H; (b) R = Me] (LXXXIII)

The dichair conformation has been assumed for the diketone (LXXXIII) on the basis of circular dichroic data[116]. In a number of studies[117,118] the dichair conformation was assumed for carbonyl derivatives of bicyclo[3,3,1]nonane without proof. There is no doubt that the problem of the conformations of 2-oxo-derivatives requires additional research. It is desirable to use for this purpose simple models, such as the ketone (LXV).

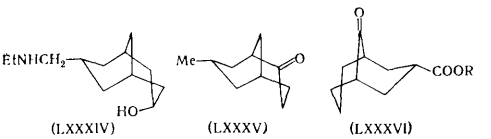
3. The Chair-Boat Conformation

We shall now consider the equilibrium (V) $\rightleftharpoons$ (VI) $\rightleftharpoons$ (VII) involving monosubstituted bicyclononanes (Section II). As stated in Section II, the introduction of a 3- (or 7-) *endo*-substituent destabilises conformation (V) and stabilises boat conformations. The problem arises of the ratio of conformations (VI) and (VII). The equilibrium position between them should be determined by two strongly destabilising 1,3-*aa*-interaction of type X... CH_2 in conformation (VII). On the other hand, in conformation (VI) the substituent occupies the bowsprit position and therefore the difference between energies of conformations (VI) and (VII) is associated with the energy of the X-*endo* $\rightleftharpoons$ X-bowsprit transition. Since the bowsprit position in conformation (VI) can be regarded as approximately equivalent to the equatorial position in conformation (VIIa), the energy difference for the (VII) $\rightleftharpoons$ (VI) transition can be estimated approximately from the energy of the (VIIa) $\rightleftharpoons$ (VI) transition. Data on the epimerisation of alcohols (XL) ($\Delta G_{OH} \simeq 2.18$ kcal mole^{-1})[52] were presented above. Thus conformer (VI) will predominate to a large extent in the conformational equilibrium; according to the data presented in Section V, the energy difference can be estimated from the energy of the X... CH_2 interaction for 1,3-disubstituted cyclohexanes.

The foregoing considerations are also valid when a choice is to be made between alternative conformations of type (X). The bowsprit position will be occupied by a substituent with more pronounced X... CH_2 repulsion. The preferred conformations of alcohols (XL)[52] and (LXXXIV)[119] confirm this postulate.

However, the above conclusion is valid only for equivalent rings in the bicyclo[3,3,1]nonane fragment. In principle, the introduction of heteroatoms can alter appreciably the energy difference between the boat and chair forms and hence disturb the above ratio of conformations (VI) and (VII). For simple mono- and di-heteroanalogues of cyclohexane, very sharp differences in this ratio are not usually observed[8,40], but in more complex cases this factor has to be taken into account.

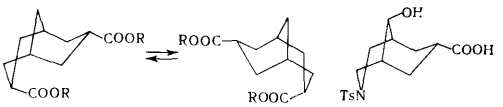
We shall consider next the influence of the nature of the 3-*endo*-substituent on the existence of this conformation. Evidently a bulky substituent such as the t-butyl group should appreciably destabilise conformation (I) and should exhibit a pronounced tendency to occupy the bowsprit position in the chair-boat conformation (II). As an example, one may compare the diester (XLIV)[67] with the epimeric ester (XLI). The 3-*endo*-methyl group also stabilises the chair-boat conformation [see compounds (XXXVIII),[66] (XXXIX),[66] and (XL).[52,66]]. It is interesting that ^{1}H NMR data for the ketone (LXXXV) indicate the existence of the normal form of the carbonyl-containing ring[68]. Furthermore, the introduction of the 3-*endo*-carboxy- or 3-*endo*-alkoxycarbonyl group also leads to conformation (II) [see compounds (XXXVI) and (XXXVII),[64] (XLII),[67] (XLV),[68] and (LXXXVI)[67]].



(LXXXIV) (LXXXV) (LXXXVI)

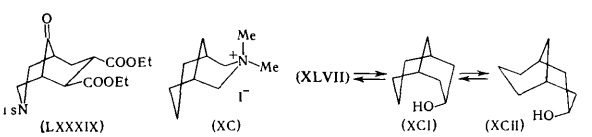
A more complex situation is observed for the dibasic acid (LXXXVIIa) and its diester (LXXXVIIb). The significant broadening of the ^{1}H NMR line at −90°C indicates the occurrence of a conformational equilibrium. However, the presence of two averaged hyperfine coupling constants J_{2a3} and J_{2e3}, both equal to 7.1 Hz, shows that the contribution of the chair-boat conformation predominates[120]. This is probably true also of other *cis*-3,7-disubstituted bicyclononanes of type (X). It has been shown for compounds (XXXII),[59,60] (XXXIII),[61] (LXVIII), and (LXIX)[68] that the introduction of a bromine atom also stabilises the chair-boat form. In the cyclohexane series the bromine atom is not regarded as a "large" substituent ($\Delta G_{Br} \simeq$ 0.38 kcal mole^{-1}),[71] since the effects of the bulk of bromine and of the length of its bond cancel out. However, in the series of bicyclo[3,3,1]nonane the bromine atom does behave as a "large" substituent.

This is true of simple heteroanalogues (see Section VI, 2). For example, the chair-boat conformation has been found for the azabicyclononanes (XXXII),[59,60] (XXXIII),[61] (LXXXVIII),[121] and (XXXIX).[101] Although the hydriodide of 3-methyl-3-azabicyclo[3,3,1]nonane[91] and the hydrochloride[91] and hydrobromide[42] of compound (XXIV) have the dichair conformation, the methiodide (XC) exists in the chair-boat conformation[91].



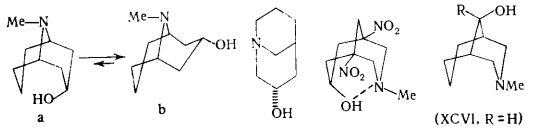
[LXXXVII, (a) R = H; (b) R = Me] (LXXXVIII)

The problem of the influence of the 3-*endo*-hydroxy-group on the preferred conformation is interesting. Firstly, this is a moderately large substituent and, secondly, the hydroxy-group can form hydrogen bonds, which can influence appreciably the position of the conformational equilibrium (see, for example, Baggett et al.[122] and Barker et al.[123]). It has been shown by ^{1}H NMR that the chair-boat conformers of 3-*endo*-bicyclo-[3,3,1]-nonanol (XLVII)[65,69,99] and of its 1,5-dimethyl derivative[79] predominate greatly. However, a study of the temperature variation of the hyperfine coupling constants and the application of shift reagents indicate the occurrence of an equilibrium[65,79,99]. However, it is not clear which form, (XCI) or (XCII), is in equilibrium with the main conformer (see also Section VII).



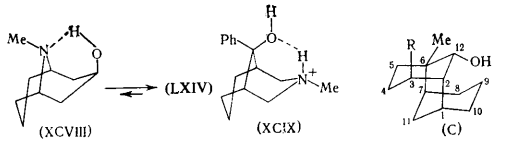
(LXXXIX) (XC) (XLVII) $\rightleftharpoons$ (XCI) $\rightleftharpoons$ (XCII)

The same problem was investigated in detail for 3α-granatanol (XCIII). Aaron et al.[89] used the method of conformational assignment based on the study of the shape of the fundamental OH stretching vibration bands in the infrared spectra. They concluded that the amines (XCIII) and (XCIV) exist in the dichair conformation. However, a detailed study of this problem showed that 3α-granatanol exists mainly in the chair-boat conformation (XCIIIb).[97-99] This is probably also true of the amine (XCIV). We may note that analysis of the band shapes in the infrared spectrum should be used with caution (see the discussion in the paper of Joris et al.[124]).



(XCIII) (XCIV) (XCV) (XCVI, R = H) (XCVII, R = Ph)

Interesting data were obtained in a study of the aminoalcohol (XCV). The infrared spectrum indicates the presence of an intramolecular hydrogen bond in this compound; thus the stabilisation of the double chair conformation by the hydrogen bond predominates over the steric repulsion due to the *endo*-functional group. This result is probably general (see Section VI, 6). It is appropriate to consider here data on the conformational equilibrium of 3β-granatanol (LXIV) and the aminoalcohol (XCVI). The infrared spectrum of the aminoalcohol (XCVI) fails to show the presence of an intramolecular hydrogen bond, which rules out the alternative chair-boat conformation[93,125]. According to ^{1}H NMR data, 3β-granatanol has the preferred dichair conformation (LXIV). However, the infrared spectrum demonstrates the presence of an intramolecular hydrogen bond, which indicates the presence of a small amount (about 11 %) of the conformation (XCVIII).[89,91] It is noteworthy that a change in conformation can occur when bicyclic amines and their derivatives are protonated (see also Section VI, 6). For example, the conformation (XCIX) has been adopted for the protonated form of the amine (XCVII), which exists in the dichair conformation[126].



(XCVIII) (LXIV) (XCIX) (C)

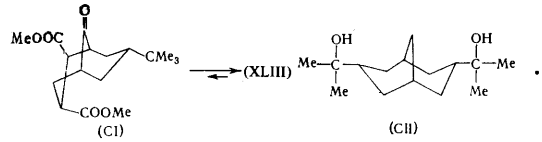
In complex polycyclic compounds the 3-*endo*-group can be constrained to form part of a dichair conformation. For example, X-ray diffraction analysis of a tricyclo-[5,3,1,1^{2,6}]dodecane (C) derivative showed that the hydroxy-group is in the *endo*-position[127]. The $C_{(9)}\ldots O$ and $C_{(4)}\ldots C_{(11)}$ distances are 2.90 and 3.09 Å respectively. Comparison of the angles shows that the hydroxy-group at $C_{(12)}$ actually causes a smaller flattening of the $C_{(8)}C_{(9)}C_{(10)}$ fragment than the $C_{(11)}$ methylene group of the $C_{(3)}C_{(4)}C_{(5)}$ fragment.

As shown in Section IV, the phosphorus-containing alcohol (XXXIV) assumes the chair-boat conformation. This conformation is determined by the strong repulsion of the two 3,7-*endo*-substituents in the dichair conformation. It is interesting that the dioxaphosphorinane ring assumes the boat form[62], probably owing to the general tendency by the P=O group to occupy the equatorial position[63].

In conclusion we may note that the problem of the conformations of bicyclo[3,3,1]nonane derivatives with a small substituent in the 3-*endo*-position is of great interest and merits a detailed study.

4. The Diboat Conformation

According to the discussion in Section II, the diboat conformation is to be expected for 3,7-disubstituted derivatives of type (IX). For a fairly bulky substituent X, the diboat conformation (XI) should be preferred rather than the chair-boat conformation (X). The ratios of forms (X) and (XI) depends on the ratio of the 1,3-*aa*-repulsion energy in the X... CH_2 fragment and the energy difference for the chair-boat conformations, which should be of the same order of magnitude in the (X) → (XI) transition as for unsubstituted cyclohexane. It has been shown for compounds (XLa),[52] (LXXXIV),[119] and (LXXXVII)[120] that the hydroxy-, carboxy-, and methoxycarbonyl groups cannot destabilise the conformation (X). However, the presence of two axial methoxycarbonyl groups in the 2- and 3-positions in the ester (CI) leads to appreciable destabilisation of the chair-boat conformation[67]. Therefore the diboat conformation (XLIII) is preferred and the methoxycarbonyl groups occupy the bowsprit and gunnel positions. It is noteworthy that the presence of the trigonal atom in the 9-position should tend to decrease the strain in the boat conformation.

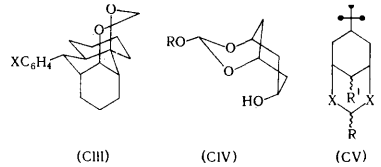


(CI) (XLIII) (CII)

^{1}H NMR showed that the diol (CII) exists in the diboat conformation[120], which is undoubtedly related to the great bulk of the substituents.

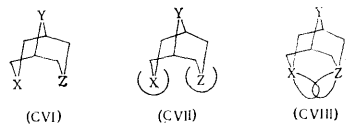
5. The Conformations of Di- and Poly-heteroanalogues of Bicyclo[3,3,1]nonane. The Problem of the Steric and Orbital Interactions of the Heteroatoms

As mentioned above (Section II), the introduction of heteroatoms into compounds of type (XV) or (XVI) can intensify the non-bonding interactions by virtue of the shortening of the C–heteroatom bond. Measurements of the dipole moments of a series of compounds of type (CIII) showed that the 1,3-dioxan ring is in the chair-boat conformation[128]. An analogous conformation was attributed to compound (CIV),[129] probably owing to the presence of the *endo*-substituent [see also compound (XXXIV)[62,63]]. The diamines (XVI, X = nitrogen) and (XXXI)[58] have the conformation of a strongly flattened dichair. Thus the problem under consideration is far from having been solved and its investigation will have to be continued in relation to simpler examples of type (CV).



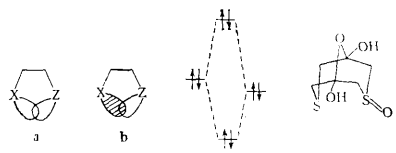
(CIII) (CIV) (CV)

An extremely interesting conformational problem arises for 3,7-diheterobicyclo[3,3,1]nonanes of type (CVI). There is no steric repulsion of the hydrogen atoms in these compounds (X and Z are nitrogen, oxygen, or sulphur).



(CVI) (CVII) (CVIII)

However, three other types of interaction can be envisaged here. Firstly a dipole–dipole (or a charge–charge) interaction. For the usual heteroatoms, this factor should lead to repulsion and its extent should diminish down the Group of elements in the Periodic System. Secondly, we have purely steric repulsion, which at short distances is associated with the repulsion of the filled electron shells as in formula (CVII). This interaction is usually described satisfactorily by Hill's formula[130,131] or by another similar expression for the interaction potential[30,132]. An interaction of this kind presupposes a spherical symmetry of the electron shells of the type present in compound (CVII) [3] (for a discussion of the "bulkiness" of the electron pair, see Robb et al.[133]). Thirdly, we have the orbital interaction called the "hockey stick effect"[16,22,134,135], illustrated in formula (CVIII). We shall consider the last problem in greater detail. For the eclipsed (or *gauche*) conformation of a disubstituted ethane fragment of type (CIX), the overlapping of orbitals leads to the formation of the bonding (CIXa) and antibonding (CIXb) combinations and the consequent splitting of the levels [formula (CX)]. Such interaction of the orbitals "through space"[22,134,136-141] leads to the destabilisation of conformation (CIX) (antibonding predominates over bonding[137,142]). An alternative conformation (for example *trans*) should arise, provided that it is allowed by structural factors. The alternative conformation for the situation illustrated in formula (CVIII) is of the chair-boat type. The degree of repulsion should be proportional to the overlapping and should increase down the Group in the Periodic System[22].



(CIX) (CX) (CXI)

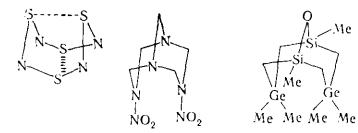
However, as shown for the first time by Hoffmann[136, 137,139], the groups X and Z can interact not only "through space" but also "through the bond", which can alter sharply the relative stabilities of the conformations[143,144]. Model compounds of the bicyclononane series can be used conveniently to isolate the orbital repulsion effect, since we can neglect the interaction between the heteratoms via four bonds.

We shall now consider experimental data on the conformations of compounds of type (CVI). Derivatives of 3,7-diazabicyclo[3,3,1]nonane (bispidine) have been studied most (see Section VI, 6). The calculated[41] and experimental[145] data for 3,7-dimethylbispidine (XXV) show that the dichair conformation predominates.

A large series of compounds of type (CVI) has been investigated[46,47,90]. In all cases where two oxygen atoms or an oxygen and a sulphur atom are present in the 3- and 7-positions [compounds (XXVIII) and (CVI) with X = Y = Z = O or X = S and Y = Z = O] the dichair conformation is preferred [for the geometry of (XXVIII), see Section IV]. However, the situation changes sharply when there are two sulphur atoms (or sulphur and selenium atoms[90]) in the 3- and 7-positions. Compound (XXXV) and compounds of type (CVI, X = Z = S, Y = CH_2; X = S, Y = O, Z = Se) exist in the chair-boat conformation[46,47,90].

It is interesting to consider the problem of the causes of such destabilisation of conformation (I). The $S_{(3)}...S_{(7)}$ distance for the hypothetical dichair conformation of (XXXV) can be calculated from the geometry of compound (XXVIII) and is found to be approximately 4.6 Å. This distance is much greater than the sums of the van der Waals radii of two sulphur atoms (3.6–3.8 Å).[146]. The experimental S...S distances are in the range 3.6–4.0 Å.[147-150] Thus the study of the geometry of molecules of type (XXVIII) and (XXXV) makes it possible to attribute the destabilisation of the dichair form to orbital repulsion.

In this connection the data of Abrahamsson and Rehnberg[147] require consideration. They found that the sulphoxide (CXI) has the dichair conformation with an extremely short $S_{(3)}...S_{(7)}$ distance of 3.17 Å. Attraction forces apparently operate between the sulphur atoms, possibly due to the positive charge on the sulphoxide sulphur atom. Examples of the stabilisation of sulphoxides and sulphones by dipole–charge attraction have been described in the literature[30,135]. We may also note that in the S_4N_4 molecule (CXII), which consists of an eight-membered ring simulating the geometry of the perimeter of the bicyclo[3,3,1]nonane molecule, there is strong attraction between two sulphur atoms, as a result of which the distance between them is 2.69 Å.[151,152]



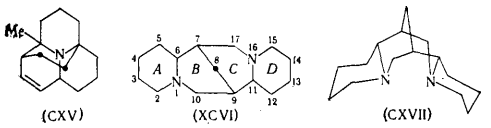
(CXII) (CXIII) (CXIV)

In conclusion of this section we may mention the conformations of polyheteroanalogues of bicyclo[3,3,1]nonane, for which only isolated and non-systematic data are available. Thus it is known that derivatives of triazaphosphabicyclononane (XXIX) [48] and tetraazabicyclononane (CXIII) [153] exist in the dichair conformation. The authors observed in the ^1H NMR spectrum of compound (CXIV) the signal of the *AB* system of the methylene protons and two signals of the methyl groups at the germanium atoms, which was used as evidence in support of the absence of an asymmetric conformation of type (II).[154] However, this reasoning is controversial and the solution of the problem requires ^1H NMR measurements at low temperatures.

6. Conformations of Alkaloids Containing the Azabicyclo[3,3,1]nonane Fragment

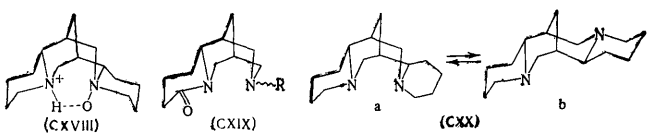
The azabicyclo[3,3,1]nonane skeleton is a component of the structures of many alkaloids. Thus the 3-azabicyclononane fragment is part of the compositions of certain diterpene alkaloids[155]; many alkaloids are also based on 9-azabicyclononane derivatives[117,156,157]. As an example, one may quote porantherine (CXV); X-ray diffraction analysis of its hydrobromide shows the presence of the 9-azabicyclononane fragment in the dichair conformation[157].

However, alkaloids of the Lupin family probably constitute the most important class. In the present section we shall consider the problem of their structures, but only in so far as this concerns the subject of the present review as a whole. Alkaloids of this group have the structure (CXVI) and as regards conformations can be divided into three groups depending on the configurations of the $C_{(11)}$ and $C_{(6)}$ centres. The dichair conformation (CXVII) should be the most stable for α-isosparteine, which has *endo*-substituents at these centres. X-Ray diffraction analysis of α-isosparteine hydrate shows that this compound does indeed have the conformation (CXVII) with an $N_{(1)} \ldots N_{(16)}$ distance of 3 Å.[158]

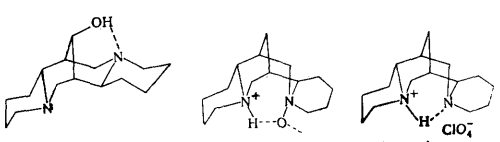


(CXV) (XCVI) (CXVII)

Next it was found that this conformation should be attributed to the cation of isosparteine *N*-oxide (CXVIII).[159,160] Despite the presence of the *endo*-substitute in (CXVIII), the dichair configuration is stabilised by the intramolecular hydrogen bond (see Section VI, 3). This is responsible for the enhanced basicity of the *N*-oxide itself, for which the dichair conformation has also been adopted[159,160]. We may also note that the dichair conformation has been attributed to various lactam structures with related configurations[156,159-163]. As an example, one may quote the tricyclic lactam (CXIX).[163] The study of the influence of the anisotropy of the nitrogen atom on the chemical shifts of the methylene protons enabled the authors to reach a conclusion about the conformation of the substituent at the nitrogen atom. The hydrogen atom occupies the axial position (CXIX, R = H), while the ethyl group occupies the equatorial position. It is not clear whether the stabilisation of the axial position of the hydrogen atom is a consequence of its small bulk or of the presence of the intramolecular hydrogen bond.


(CXVIII) (CXIX) a (CXX) b

We shall now formulate the conformational problem which arises for alkaloids of the sparteine series (we believe that in a number of studies it was artificially made more complicated[164,165]). On the basis of the foregoing considerations, two conformations (CXX, a and b) can be postulated for sparteine (CXX). One of them includes a bicyclononane fragment in the dichair conformation but has an axial substituent at $C_{(11)}$ and therefore a *cis*-junction of the *C* and *D* rings of the quinolizidine fragment. *A priori* estimates of the stabilities of these conformations are difficult owing to the lack of data on conformational equilibria in model quinolizidine systems. It is known only that *trans*-quinolizidine is more stable than the *cis*-isomer, but the available quantitative data are subject to a scatter of 2.1—4.6 kcal mole^{-1}.[166-169]

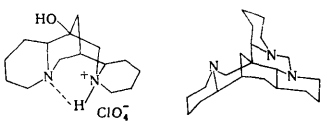

(CXXI) (CXXII) (CXXIII)

Infrared spectroscopic and ^{1}H NMR studies on compounds with the sparteine skeleton[161,162,164,170,171] showed that the *C* ring has the preferred boat conformation (CXXb). This is shown particularly clearly by the hyperfine coupling constant $J_{H_{(7)}H_{(17)}} = 10$ Hz.[164] The chair-boat conformation has also been demonstrated for 8-hydroxysparteine (CXXI)[170] by the presence of the intramolecular hydrogen bond.

However, the difference between the free energies of conformations (CXXa) and (CXXb) is probably relatively small. At any rate the formation of complexes via the two nitrogen atoms, which is possible only in the dichair conformation, may alter appreciably the position of the conformational equilibrium. Such coordination takes place, for example, when sparteine reacts as a bidentate ligand with organolithium[172] or organoaluminium compounds[173], which permits asymmetric syntheses. Incidentally, this indicates the necessity for caution in the employment of shift reagents in ^{1}H NMR conformational studies on compounds of this series.

The hydrogen bond has a similar effect. Thus the sesquiperchlorate of sparteine *N*-oxide (CXXII) exists, like compound (CXVIII), in the dichair conformation owing to the presence of the intramolecular hydrogen bond[174,175]. Borovyak et al.[176] obtained an extremely interesting result. They showed by X-ray diffraction of sparteine monoperchlorate (CXXIII) that this salt assumes the dichair conformation with a distance between the nitrogen atoms of only 2.79 Å. The sharp difference between the conformations of sparteine (in solution) and of its salt (in the crystalline state) can be attributed either to the difference between the states of aggregation or to the stabilisation of the dichair conformation by the intramolecular hydrogen bond on protonation of one nitrogen atom. It would be useful to undertake a study of the conformations of sparteine salts in solution.

There are few data on the conformations of β-isosparteine. The dichair conformation has been adopted for this compound[170]. The same conformation has been found for the monoperchlorate of the 7-hydroxy-derivative of (CXXIV) in the crystalline state[177]. However, it is possible that the presence of the hydrogen bond alters in this case too the conformational pattern characteristic of the free base.


(CXXIV) (CXXV)

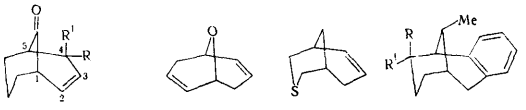
The chair-boat conformation has been found for the azabicyclononane fragment of compound (CXXV).[178] These data were obtained for the free bases and all complicating factors (for example, hydrogen bonds) are absent. Therefore the *trans*-junction of the quinolizidine fragment is probably a more important factor for conformational specificity than the dichair conformation.

7. Conformations of Unsaturated Derivatives of Bicyclo-[3,3,1]nonane and Its Heteroanalogues

The introduction of a double bond into the bicyclo[3,3,1]-nonane skeleton leads to a fairly marked distortion of the geometry. The presence of the 2,3-double bond [compound (XIII)] leads to a sharp decrease of the 3—7 repulsion owing to the flattening of the cyclohexene ring.

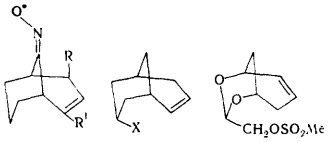
Evidently the saturated ring will have the chair conformation. By virtue of the rigid junction between the rings and the requirement that the $C_{(1)}C_{(2)}C_{(3)}C_{(4)}$ fragment must be planar, the cyclohexene ring in compound (XIII) should be rigid and incapable of inversion.

Experimental data confirmed this hypothesis. A marked flattening of the unsaturated ring in the epimeric ketones (CXXVI) and (CXXVII) has been indicated by J_{45}(CXXVI) = 6.4 Hz and J_{45}(CXXVII) = 0 [179] (cf. Zefirov and Rogovina[90], Section VI, 1).



(CXXVI, R = Ph, R' = H) (CXXVII, R = H, R' = Ph) (CXXVIII) (CXXIX) (CXXX)

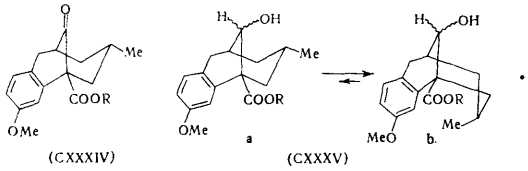
A similar flattening has been observed also in the diene (CXXVIII).[90] A conformation of type (XIII) has also been found for heteroanalogues [the sulphide (CXXIX) [90]], benzo-derivatives [compounds of type (CXXX) [180]], and stable free radicals of type (CXXXI) [181] [cf. compounds (LXXX) and (LXXXI), Section VI, 2].



(CXXXI) (CXXXII) (CXXXIII)

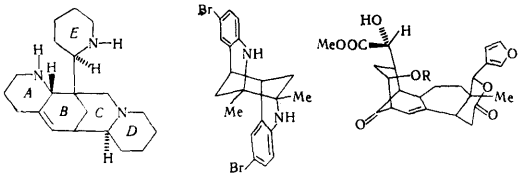
However, the conformational problem specific to the unsaturated compounds of the series under consideration is of greatest interest. It can be formulated as follows: since the unsaturated ring is appreciably flattened, it is interesting to discover whether the chair conformation of the saturated ring is retained in the presence of a 7-*endo*-substituent in compounds of type (CXXXII).

There are few available literature data but they nevertheless lead to the definite conclusion that there is a sharp decrease of 3—7 repulsion in systems of type (CXXXII). For example, the chair conformation has been attributed to the methanesulphonate (CXXXIII).[129] Interesting data have been obtained by Colvin et al.[182] The methyl group in compounds (CXXXIV) and (CXXXV) gives rise to a doublet in the ^{1}H NMR spectrum with δ = 0.8 and 0.4 p.p.m. respectively. The difference of 0.4 p.p.m. can be accounted for as follows. The methyl group in compounds (CXXXIV) is remote from the benzene ring, because the saturated ring assumes the boat conformation. Reduction of the carbonyl group leads to the appearance of flagpole—flagpole repulsion in the boat conformation, which results in an equilibrium between (CXXXVa) and (CXXXVb) and a shift of the methyl group signal owing to the steric proximity of the benzene ring. This is confirmed by the chemical shift of the compounds epimeric with respect to the methyl group, which evidently have the chair conformation in both cases[182].



(CXXXIV) (CXXXV)

The chair conformation has been found for the nitrogen-containing ring in the azabicyclononane fragment in podopetaline hydrobromide (CXXXVI).[183] The *A*, *D*, and *E* rings also have the chair form, but the *B* ring assumes the "sofa" conformation[183-186]. Thus there is a *cis*-junction between the *C* and *D* rings of the quinolizidine fragment of this compound, while in the saturated alkaloid (CXXV) there is a *trans*-junction[178] (see Section VI, 6). This example clearly demonstrates a decrease of the 3—7 repulsion for unsaturated systems of the type under consideration. There are data for the geometries of other complex compounds, for example the diamine (CXXXVII) [187] or the *p*-iodobenzoate of destigloylswietenine (CXXXVIII).[188,189] We may note that compounds of type (CXXXII) have recently become relatively readily available[190,191], so that it would be desirable to investigate the problem under consideration quantitatively on simple models.



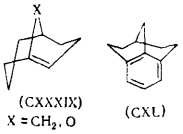
(CXXXVI) (CXXXVII) (CXXXVIII)

The syntheses of compounds of type (CXXXIX) containing a double bond at the bridgehead were described recently[192-196] and the limitations of Bredt's rule were thus demonstrated. The unsaturated ring in these structures should be a rigid half-boat in which the requirement of minimum twisting of the double bond is met. The saturated ring should have the chair form. We may note an interesting aromatic hydrocarbon (CXL).[197] Although the authors postulate the existence of several possible conformers, this does not appear to be a realistic assumption, because (CXL) should have a unique rigidly fixed structure.

VII. CONFORMATIONS AND REACTIVITIES OF BICYCLO-[3,3,1]NONANE DERIVATIVES

In this section we shall consider briefly the possibility of applying chemical methods of bicyclo[3,3,1]nonanes and their reactions will be discussed.

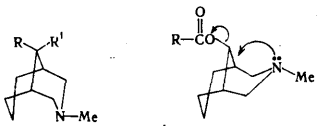
Information about the preferred conformations can be obtained from kinetic and stereochemical data. For example, the similarity of the relative rates of solvolysis of the epimeric *p*-nitrobenzoates (CXLI) and (CXLII) confirms that the dichair conformation is preferred, because in the chair-boat conformation one might expect a synartetic acceleration of solvolysis for the *anti*-epimer (CXLIII).[125,126,198]



(CXXXIX) X = CH_2, O (CXL)

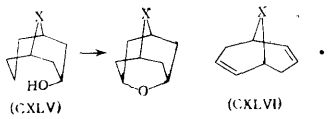
A similar addition of organomagnesium compounds to the ketone (LXXIX) leads to almost equal fractions of the

epimeric alcohols (CXLIV), a and b, which is also logical for the dichair conformation[126].



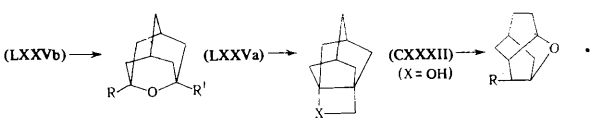
(CXLI, R = *p*-$NO_2C_6H_4COO$; R^1 = H)
(CXLII, R = H; R^1 = *p*-$NO_2C_6H_4COO$)
(CXLIII)
[CXLIV, (a) R' = OH; (b) R = OH]

Bearing in mind the non-bonding $H_{(3)} \ldots H_{(7)}$ interaction, compounds of the bicyclo[3,3,1]nonane series will presumably be converted into derivatives with adamantane-like structures. Evidently such conversion takes place in the dichair conformation. For example, the oxidation of alcohols of type (CXLV) by lead tetra-acetate is accompanied by cyclisation to oxa-adamantane derivatives[99,199].

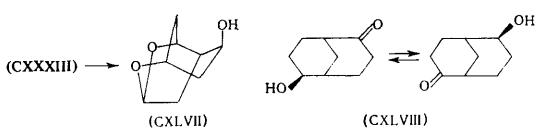


(CXLV) (CXLVI)

A wide variety of numerous transformations of 3,7-functional derivatives of bicyclo[3,3,1]nonanes into derivatives with an adamantane structure are known[200-207]. We may quote, for example, the cyclisation of dienes of type (CXLVI) and the diketone (LXXVb) to oxa-adamantane derivatives, of the methylene derivative (LXXVa) to noradamantane derivatives, and of the enol (CXXXII, X = OH) to isoadamantane derivatives[201-207].

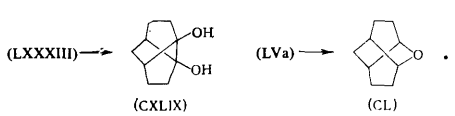


We may also note that the cyclisation of the methanesulphonate (CXXXIII) to the tricyclic compound (CXLVII) is one of the stages in the total synthesis of prostaglandin $F_{2\alpha}$.[129]



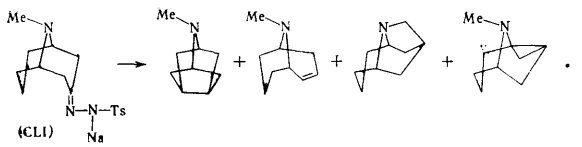
(CXLVII) (CXLVIII)

The steric proximity of the 3,7-positions makes hydride transfer possible[191,207,208]. Deuterium exchange involving the ketol (CXLVIII) indicates the occurrence of an intramolecular stereospecific 2—6 hydride shift[210]. The transition state in this reaction should include the diboat twist-conformation. We may also note the cyclisation of the diketone (LXXXIII) to a pinacol[7], which has the nortwistane skeleton, and also the cyclisation of the diol (LVa) to oxatwistane (CL).[211] These are not exhaustive examples, showing merely how the bicyclo[3,3,1]nonane fragment can react.



(CXLIX) (CL)

Naturally, conformational assignments on the basis of the structure of the products obtained must be made with caution, because the energies of conformational transitions are usually small compared with activation energies. We may point out, for example, that the decomposition of the tosylhydrazone (CLI) leads to a complex mixture of products, including some with a fixed chair-boat conformation[212,213].



(CLI)

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It follows from the foregoing data that the bicyclo-[3,3,1]nonane system is a convenient model for the solution of a large set of problems in conformational analysis. In particular, the possibilities provided by this model for the investigation of the reactivities of functional groups in the boat conformation or of problems concerning the transannular interactions of heteroatoms and functional groups are frequently completely unique. There is no doubt that the great possibilities of this system in relation to problems of conformational analysis will be ultilised in the future.

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New Ideas on the Mechanism of Direct Syntheses of Alkyl(aryl)chlorosilanes

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Studies on the direct syntheses of alkyl(aryl)chlorosilanes, which have served as a basis for the development of new ideas on the reaction mechanism formulated mainly in the last 2-3 years, are reviewed. The direct syntheses are used in the industrial manufacture of the most important organosilicon monomers. The new ideas on the mechanism proved to be extremely useful in determining the rules for the control of technological processes. The ideas concerning the specific role of chlorine transfer processes and the chain mechanism of the formation of alkyl(aryl)chlorosilanes which are discussed here were not dealt with in the previous reviews.
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I. INTRODUCTION

Data on the reaction kinetics and the adsorption of gaseous reactants are examined in detail in the published reviews on the mechanisms of the direct syntheses of alkyl(aryl)-chlorosilanes[1-5], but other extremely important aspects of the reaction mechanism are discussed inadequately, since they began to be considered in the literature only in the last few years. These aspects are the decisive role and mechanism of chlorine transfer from the organic chloride to silicon and also the composition and importance of the surface intermediates.

The ideas developed in the above investigations explained the observed findings and in many cases made it possible to formulate the research needed to intensify and improve the direct syntheses, which constitute the foundation of the industrial manufacture of the principal organosilicon products[6,7].

The direct synthesis of alkyl(aryl)chlorosilanes is an extremely complex and specific heterophase catalytic process in which a multicomponent mixture of compounds is formed and the properties of the solid reactant change significantly in the course of the reaction. For this reason, chemical methods were resorted to (and proved to be fruitful) together with physical and physicochemical procedures. The extensive experimental data accumulated in the development of technological processes also proved to be very useful.

The results of the main studies devoted to the mechanism of the direct syntheses of alkyl(aryl)chlorosilanes are surveyed in the present review in the light of new ideas.

II. SURFACE INTERMEDIATES—PRODUCTS OF THE PARTIAL CHLORINATION OF SILICON

The bonds linking silicon atoms in the crystal lattice are extremely strong (the heat of sublimation of silicon is 110 kcal mole^{-1})[8] and are broken only under the influence of powerful reagents, for example halogens, hydrogen halides, or alkalis. The breakdown of the silicon crystal lattice, which is necessary for the reaction with organic chlorides, also begins in all probability with attack on its surface atoms (primarily those with unsaturated valences, of which there are about 10% according to Haneman[9]) by chlorine. The affinity of silicon for chlorine is illustrated, in particular, by the high strength of the Si–Cl bond (85 kcal mole^{-1} compared with 58 kcal mole^{-1} for the Si–C bond[10]).

In the absence of a catalyst, direct syntheses of alkyl-(aryl)chlorosilanes begin only when chlorine or hydrogen chloride is introduced or at the decomposition temperature of the organic chloride, especially with evolution of hydrogen chloride[11-17]. Therefore a decrease of the decomposition (dehydrochlorination)[18] temperature in the series of alkyl chlorides with increase in the size of the alkyl group is correlated with the decrease of the temperature of the direct synthesis of the corresponding alkylchlorosilanes (the yields of $RSiHCl_2$, $RSiCl_3$, and $HSiCl_3$ are then higher and those of R_2SiCl_2 are lower than in the synthesis of the lowest alkylchlorosilanes[19-22]). The introduction of hydrogen chloride[23-32] or its additional formation in the reaction zone[7,33-35] as a rule accelerates the processes sharply.

Therefore studies dealing with the induction period in the direct syntheses are of considerable interest[36-38]. Investigations by pulse chromatography showed that the induction period is due primarily to the decomposition reactions of the organic chloride; chlorine is then fully bound to the surface of the solid reactant. In the desorption from the solid surface at the end of the induction period at 450 to 600°C, a relatively large amount of trichlorosilane and silicon tetrachloride, which appear to be the main products of the secondary reaction[39], is removed and chlorine and hydrogen chloride are evolved in very small quantities. The formation of alkyl(aryl)chlorosilanes at an appreciable rate begins when a definite amount of bound chlorine is present on the solid surface[38]. Therefore preliminary treatment of the solid reactant by chlorinating agents leads to a decrease of the temperature of the start of the formation of alkyl(aryl)chlorosilanes in the subsequent reaction between the solid and the organic chloride. The removal of chlorination products leads to the deactivation of the solid reactant, while its repeated treatment by chlorine or hydrogen chloride restores its reactivity[37,40].

In a number of studies[11,12,41-51], starting with those of the discoverer of the direct synthesis (Rochow)[11], the involvement of intermediates—products of the partial chlorination of silicon of the type of $SiCl_n$ (where $n < 4$) and HSiCl, was postulated.

Assuming the involvement of organic radicals in the formation of alkyl(aryl)chlorosilanes, Rochow showed that methyl radicals obtained from tetramethyl-lead add to chlorinated silicon only (chloromethylsilanes, which are formed as long as chlorine is present on the surface, were subsequently also detected[52] at 500°C in the reaction of dimethyl ether with a silicon–copper alloy subjected to preliminary treatment with hydrogen chloride). However, this reaction does not occur with $SiCl_4$. On this basis, Rochow proposed a mechanism for the formation of alkyl(aryl)chlorosilanes with participation of partial silicon chlorination products. Similar views on the mechanism of the direct synthesis were expressed by other investigators[45–47]. Czech investigators used the concept of the involvement of the surface compound $SiCl_2$ in devising mechanisms for the formation of $HSiCl_3$ (Joklik and Bažant[43]) and CH_3SiCl_3 (Joklik and Bažant[44]).

The experimental data for the direct syntheses, on which a mechanism of the formation of chloromethylsilanes, chloroethylsilanes, and trichlorosilane with participation of the compounds $SiCl_n$ and HSiCl can be based[12,42,53], were subsequently confirmed by kinetic studies[48–50,54].

There are literature data for the formation of the partial silicon chlorination product $SiCl_2$ by the reaction of silicon tetrachloride with silicon above 1000°C[55–66] and also by the pyrolysis of trichlorosilane, hexachlorodisilane, or perchloropolysilanes[67–69]. The results of kinetic[56], spectroscopic[60], and mass-spectrometric[61] studies on this compound have been published. It has been established that dichlorosilylene can be readily inserted in an M–Cl bond (M = B, P, or C)[70]; when it reacted with methyl chloride in the presence of copper at 350°C, it was possible to obtain chloromethylsilanes[71]. Interesting synthetic possibilities involving the use of dichlorosilylene for the preparation of organosilicon heterocyclic compounds[67,69] and other substances[72] have been demonstrated. The preparation and properties of the chloropolysilanes $(SiCl)_x$,[73] $(SiCl_2)_x$,[71,74], etc.[75–78] have been studied.

In an investigation[79] of the mechanism of the chlorination of metals it was claimed that the addition of chlorine takes place in the gas phase as a result of the reaction with the metal vapour which is always present at the surface. On the other hand, other workers[80] believe that the chlorination of silicon takes place on the surface with participation of atoms linked to one another. It has been stated[41] that the first chlorine atom adds to silicon in the solid phase and the remaining silicon valencies are saturated in the gas phase.

Mass-spectrometric studies on the products of the reaction of silicon with chlorine[81], hydrogen chloride[82], and copper(I) chloride[83] demonstrated the formation on the surface of SiCl, $SiCl_2$, and $SiCl_3$, which can escape into the gas phase under certain conditions[82–84]. The possibility of the existence of gaseous SiCl, $SiCl_2$, and $HSiCl_2$ was confirmed by thermodynamic calculation and the existence of $SiCl_2$ was confirmed by ultraviolet spectroscopic data[85].

The products obtained by the partial chlorination of silicon can react with methyl chloride after being desorbed into the gas phase[42]. However, the gas-phase reactions are apparently unimportant for the direct synthesis: studies on the kinetics and mechanisms of the reactions lead to the conclusion that the formation of hydrogen-containing and alkyl(aryl)chlorosilanes is a purely heterogeneous process[21,86–94]. The application of the method involving separate calorimetric measurements[95–98] showed that all the exothermic stages of the processes take place on the surface. Consequently the main bulk of the products of the partial chlorination of silicon react in the direct synthesis as surface compounds. Recent studies yielded experimental data on their properties, compositions, and role in the overall processes involved in the direct synthesis.

It has been shown that products obtained by the chlorination of the silicon surface are comparatively stable both at room temperature and at the temperatures of the syntheses. It has been established mass-spectrometrically that, even several hours after formation, they can be desorbed from the surface by hydrogen chloride in the form of trichlorosilane close to room temperature[82] or by evacuation at an increased temperature[39]; they can be fully desorbed only after heating the specimens at 600°C for many hours[37] (the claim that the desorption ceases after the specimens of chlorinated silicon have been heated at 310°C[82] is inconsistent with the results of experiments in which the chlorination products were involved in the reactions at temperatures of about 500°C[37,52]).

To determine the nature and compositions of these compounds, formed directly in the reaction zone under the conditions of direct synthesis, the silicon surface containing the partial chlorination products was methylated by methylmagnesium chloride and was rechlorinated after the removal of magnesium chloride; a mixture containing CH_3SiCl_3, $(CH_3)_2SiCl_2$, and $(CH_3)_3SiCl$ was formed[99]. The interaction of chlorinated silicon with the Grignard reagent to form an $Si-CH_3$ group is possible only in the presence of a covalent bond between chlorine and silicon. On this basis, the authors concluded that the chlorination of silicon, which is responsible for the sharp increase of its reactivity in the subsequent reaction with an organic chloride, leads to the formation of the surface intermediates SiCl, $SiCl_2$ and $SiCl_3$ [corresponding to the formation of CH_3SiCl_3, $(CH_3)_2SiCl_2$, and $(CH_3)_2SiCl$].

The presence of the surface compounds $SiCl_n$ alters significantly the state of the surface and its adsorption properties. Adsorption studies by the contact potential difference (CPD) method showed that the chemisorption of the organic chloride from the solid reactant surface in the positively charged β-form is the initial stage of the direct synthesis responsible for the weakening of the bond between silicon (acceptor) and the crystal lattice[100–103]. After treating a silicon–copper alloy (2.4% Cu) with hydrogen chloride at 150°C, the nature of the subsequent chemisorption of hydrogen chloride on the alloy changes appreciably, in particular the positively charged form of the adsorbate becomes more stable[104]. The strengthening of the adsorption linkage between HCl and the silicon–copper alloy (8.63%) after its exposure to an atmosphere of HCl is also indicated by chromatographic data[105].

The presence of Si–Cl bonds on the silicon surface promotes more active chemisorption of methyl chloride on the latter. The desorption of the chlorination product as a result of the heat treatment of the specimen *in vacuo* lowers its adsorption capacity, which is reduced to a minimum after heating at 1150°C; the synthesis of chloromethylsilanes directly afterwards promotes the restoration of the adsorption capacity of the specimen[46]. To a first approximation, the adsorption of methyl chloride on the chlorinated specimen in the β-form active in the direct synthesis corresponds to a change in the surface potential, which is approximately twice as large as in adsorption on the nonchlorinated specimen[106].

Some authors[106–108] believe that the compounds $SiCl_n$ are responsible for the formation of active centres on which the reacting organic chloride molecule is adsorbed: its interaction with silicon is facilitated by the presence of an electronegative substituent at the silicon atom in the crystal lattice. It has been shown[107] that, when silicon is treated with hydrogen fluoride rather than hydrogen chloride, the

temperature of the start of its reactions with methyl chloride is reduced even more: the higher electronegativity of fluorine present as a substituent at the silicon atom facilitates to a greater extent the interaction of the halogenated silicon with methyl chloride. One of the causes of this is the stronger bond between the chlorine atoms of the adsorbed organic chloride molecules and the halogenated silicon atoms on the surface compared with the non-halogenated atoms. Bonds involving *d* orbitals (in particular chemisorption bonds) are known to be strengthened when electronegative substituents are attached to silicon[109] (in our case chlorine). The strengthening of the adsorption linkage between the organic chloride and silicon weakens the bonds between the silicon atom and the crystal lattice and is a necessary condition for the rupture of these bonds[106].

In the latest systematic studies on the kinetics and mechanisms of the reactions of HX[4,5,48,104,110–112] and CH_3X[4,5,111] (X = Cl or Br) with silicon and germanium the idea that the M–M bond strength (where M = Si or Ge) determines the rate of the direct synthesis of hydrogen-containing silanes and germanes, halogenomethylsilanes, and halogenomethylgermanes has been developed. In support of these views, the authors quote in the first place the following evidence: (1) the decrease of the reaction temperature and activation energy with increase in the amount of impurities in silicon facilitating the dissociation of the Si–Si bonds in the transition state[48,104,113]; (2) the increase of the plasticity of the surface layers of single-crystal silicon due to the decrease of the specific surface energy of the crystal and hence of the Si–Si bond strength as a result of the introduction of microamounts of copper (0.0013–0.3%), which tend to increase the reactivity of silicon in the synthesis of trichlorosilane and dichloromethylsilane[111]; (3) the similarity of the kinetic characteristics of the reactions of silicon or germanium with HX or CH_3X regardless of the nature of the halogen (chlorine or bromine)[4,5,110]; (4) the correlation between the Si–Si and Ge–Ge bond strength on the one hand and the activation energy of the chlorination of hydrobromination of silicon and germanium on the other [112]; (5) the parallel variation of the activation energies for the synthesis of trichlorosilane or trichlorogermane with M–M bond strengths following the introduction of germanium into silicon or conversely[5]. All these findings are satisfactorily consistant with the postulated involvement of surface compounds containing Si–Cl bonds, which weaken the bonds between silicon atoms and the crystal lattice, in the formation of active centres.

These ideas are also confirmed by results[100,103] obtained in studies of the chemisorption of various chloro-derivatives on solid reactants treated with hydrogen chloride at 450°C, i.e. containing the surface products of the partial chlorination and hydrochlorination of silicon, although the authors assume without experimental evidence that the chemisorption takes place at silicon atoms.

Surface compounds of the type SiX_n are directly involved in the formation of the final products of the direct synthesis. This has been confirmed experimentally[99,107]. In the reaction of methyl chloride with the surface of silicon treated with hydrogen fluoride, the products are fluoromethylsilanes and chlorofluromethylsilanes[99]. An increase in the degree of preliminary chlorination of silicon leads to an increase of the amount of chloromethylsilanes obtained in the reaction between silicon and methyl chloride injected in a single pulse under conditions which virtually rule out the supplementary formation of the compounds $SiCl_n$.[107]

The products of the partial chlorination of silicon on the surface also serve as active centres for the decomposition of the organic chloride. For example, in the interaction of methyl chloride with chlorinated silicon, even under the conditions of a very low degree of chlorination where chloromethylsilanes still cannot be detected, the amount of hydrocarbons is significantly greater than in the reaction with non-chlorinated silicon[107].

Ideas concerning the composition of the products of the partial chlorination of silicon and the mechanism of their involvement in the formation of alkyl(aryl)chlorosilanes (with and without catalysts), which follow from experimental results, were first put forward in a study of the synthesis of chlorophenylsilanes (for R_2SiCl_2 and $RSiCl_3$)[108,114] and chloroethylsilanes (for $RSiHCl_2$ and partly $RSiCl_3$)[12].

Subsequently the identification of fluoromethylsilanes and chlorofluoromethylsilanes, obtained in the reaction of methyl chloride with solid reactant surfaces subjected to a preliminary treatment with hydrogen fluoride, confirmed the above hypothesis[99]. The possibility of the involvement of SiX, SiX_2, and SiX_3 in the formation of $RSiX_3$ and of SiX in the formation of R_2SiX_2 was demonstrated; the formation of $RSiHX_2$ with participation of HSiX cannot be ruled out. CH_3SiFCl_2, CH_3SiF_2Cl, CH_3SiF_3, and $(CH_3)_2SiFCl$ were clearly identified and $CH_3SiHFCl$ and $(CH_3)_3SiF_2$ were tentatively identified in the reaction of methyl chloride with surface compounds of the type SiF_n. Additional data for the compositions of the intermediates in the direct synthesis were obtained in a study of the interaction between dimethyl ether and the surfaces of solid reactants treated with Cl_2 or HCl.[115] The compound $HSiCl_2$ (corresponding to CH_3SiHCl_2 detected in the products), which is probably involved in the formation of $RSiHCl_2$, can exist on the surface together with SiCl, $SiCl_2$, $SiCl_3$, and HSiCl. In another investigation the silicon surface was treated with hydrogen chloride or chlorine under the conditions of the preferential formation of products of the partial chlorination of silicon on the surface: SiCl or $SiCl_2$ and $SiCl_3$. $(CH_3)_2SiCl_2$ or CH_3SiCl_3 respectively predominated in the products of the reaction of methyl chloride with the surface of the chlorinated silicon specimens[107].

Since different final products can be formed (depending on the properties of the solid reactant and the reaction conditions) in reactions involving the same surface compound (see p.15), a clear correlation between the composition of the compounds $SiCl_n$ and the final reaction products is on the whole impossible. Thus, under the conditions of rapid decomposition of organic chlorides, the compounds SiCl are gradually converted into $SiCl_3$, participating ultimately in the formation of $RSiCl_3$. The same applies to the compounds $SiCl_2$. If the rate of decomposition is low and the reactivity of the solid with respect to the formation of the Si–C bond is adequate (mainly in the presence of a catalyst), the compounds SiCl are probably involved mainly in the formation of R_2SiCl_2 and the compounds $SiCl_2$ are involved in the formation of alkyl(aryl)trichlorosilanes[99,108].

III. THE MECHANISM OF CHLORINE TRANSFER FROM THE ORGANIC CHLORIDE TO SILICON

1. The Transfer of Chlorine in the Formation of Individual Alkyl(aryl)chlorosilanes.

A seemingly paradoxical increase not only of the overall reactivity but also of the selective reactivity of the solid reactants in the formation of dialkyl(aryl)chlorosilanes (compounds with a relatively low chlorine content) after the introduction into the reaction of small amounts of chlorine or chlorine donors (HCl, CuCl, $HSiCl_3$, etc.) has been observed

in studies on the synthesis of chloromethylsilanes[7], chloroethylsilanes[53], and chlorophenylsilanes[106,114,116,117]. For example, the addition of 0.5–1.5% CuCl increases the yield of dichlorodiethylsilane by 25–30%[53,85] and the addition of water, which leads to the formation of hydrogen chloride in the reaction zone, increases the yield by a factor of 1.5.[53] Fig. 1 illustrates the influence of added hydrogen chloride on the reaction of chlorobenzene with a solid reactant consisting of a mixture of silicon and copper powders (40%)[108]. With increase of hydrogen chloride concentration in the reaction mixture to 12%, the rate of formation of dichlorodiphenylsilane increases approximately by a factor of five, despite the fact that hydrogen chloride is not involved in the overall reaction whereby it is synthesised.

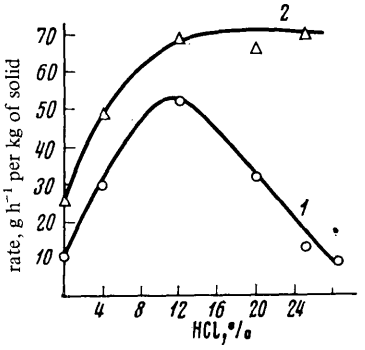


Figure 1. Variation of the rates of formation of dichlorophenylsilane (curve *1*) and trichlorophenylsilane (curve *2*) as a result of the introduction of hydrogen chloride in the synthesis of the chlorophenylsilanes on a mixture of silicon and copper powders.

In the direct synthesis of trichlorophenylsilane without a catalyst (at about 600°C with the ratio HCl : C_6H_5Cl = 1 or 4–1.8)[7,15], hydrogen chloride is again not involved in the overall reaction scheme, in contrast to other processes for the synthesis of alkyl(aryl)trichlorosilanes[37,118]: the yield of trichlorophenylsilane is about one mole for three moles of the chlorobenzene which has reacted and the overall amount of silicon tetrachloride and trichlorosilane corresponds to the amount of hydrogen chloride which has reacted. In the absence of hydrogen chloride, the reaction barely proceeds (the degree of conversion of chlorobenzene does not exceed 5%).

Such experimental results suggested that chlorine or chlorine donors, in particular CuCl and HCl which react with silicon to form the surface compounds $SiCl_n$, initiate the process, the compounds $SiCl_n$, which serve as the active centres for the reaction, being regenerated[106,108]. Similar ideas about the mechanism of the formation of dialkyldichlorosilanes were put forward in early investigations[53,85], where it was found that the amount of chlorine in dichlorodiethylsilane, formed when ethyl chloride interacts with chlorinated silicon in the absence of a catalyst, greatly exceeds the amount of chlorine combined in the preliminary chlorination of silicon.

The employment of pulse chromatography yielded an experimental confirmation of these ideas about the direct syntheses[99,107].

Silicon tetrachloride and chloromethylsilanes were detected together with chlorofluoromethylsilanes when silicon treated with hydrogen fluoride was allowed to react with methyl chloride at 350–450°C. The interaction of methyl chloride with non-halogenated silicon atoms is virtually ruled out under these conditions. Therefore the formation of halogeno-derivatives of silicon without fluorine might have been a consequence only of the addition of chlorine to silicon atoms adjoining the SiF_n surface species, i.e. a consequence of the regeneration of the surface compound — a product of the partial chlorination of the adjoining silicon atom after the completion of the cycle involving the formation of alkyl(aryl)chlorosilanes[99].

The deactivation of the solid reactants after the desorption of $SiCl_n$ and the restoration of their reactivity on chlorination show that constant regeneration of these compounds during synthesis is a necessary condition for the retention of the reactivity of the solid reactant in the course of the entire process[106].

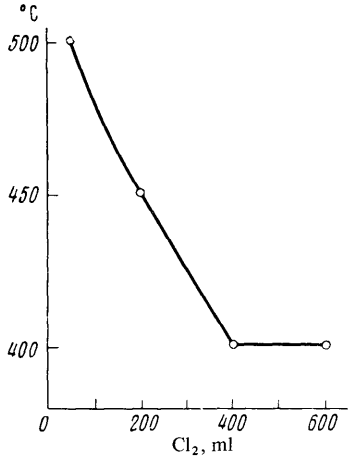


Figure 2. Effect of the degree of chlorination of silicon on the measured temperature of its steady reaction with methyl chloride.

It is very significant that preliminary chlorination of silicon lowers not only the temperature of the beginning of its reaction with methyl chloride but also the temperature of the development of the process in which the rate of the reaction already begun does not decrease during subsequent injections of methyl chloride. An increase in the degree of chlorination lowers the observed temperature of the steady reaction involving the formation of chloromethylsilanes (Fig. 2)†. Since a steady reaction requires that the products of the partial chlorination of silicon be replenished and

† The gradual inhibition of the formation of trichloromethylsilane and $SiCl_4$ as $SiCl_n$ is removed, observed[37] in the reaction of methyl chloride with the surface of chlorinated silicon at 350–500°C, is associated with the fact that the chlorination was carried out with 200 ml of chlorine at 350°C; Fig. 2 presents the results of experiments with specimens chlorinated at 400°C.[107]

at the temperatures considered (below 600°C) the decomposition of methyl chloride on silicon with formation of $SiCl_n$ is negligible, evidently $SiCl_n$ is renewed in the course of the reaction itself[107]. Only the decomposition of RCl [without the formation of alkyl(aryl)chlorosilanes] on the active centres leads to the ultimate formation of chlorosilanes alone and is not accompanied by the generation of new active centres.

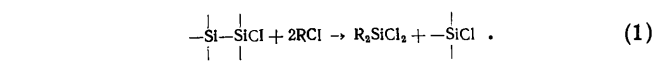
Semenov, Voevodskii, and Vol'kenshtein[119–121], Roginskii[122], and others[123] developed hypotheses concerning heterogeneous-catalytic processes with surface or fixed chains, occurring on repetition of reaction cycles at the active centres formed previously on the catalyst surface. Such views are close to those concerning the catalytic process involving a non-stoichiometric initiator, for example carbon monoxide, in the hydropolymerisation of olefins on a cobalt catalyst[124–126]. Polymerisation, initiated hydropolymerisation, and the synthesis of hydrocarbons from CO and H_2 are nowadays classified as catalytic processes involving the formation of surface chains[127].

The study of the mechanism of the direct synthesis of alkyl(aryl)chlorosilanes suggests that many reactions involved in this process, which are of greatest practical importance, can be classified as catalytic heterophase reactions with surface chains proceeding with participation of an initiator[99,106–108,114]. The initiators can be chlorine or chlorine donors (CuCl and HCl). They form surface compounds of the type $SiCl_n$ (by partial chlorination of silicon), which are involved in the formation of active centres for the reaction. The chemisorption and subsequent reaction of the organic chloride at the active centres lead to the formation of the final reaction products with regeneration of the active centre at an adjoining silicon atom. The cycle is completed by the desorption of the final product into space and the regeneration of $SiCl_n$ is accompanied by the liberation of other silicon atoms, whose valencies probably remain free and which are thus available for the surface reaction. The characteristic features of the direct synthesis are the formation of initiators (chlorine compounds) in the reaction zone on decomposition of the organic chloride and also the possibility of the occurrence of reactions with participation of initiators introduced from outside.

The data concerning the chain mechanism of the direct synthesis are consistant with the theoretical postulates concerning the chain mechanisms of reactions on the surface of solids. However, an unambiguous confirmation of this requires certain additional quantitative studies, which are of fundamental interest for the solution of general problems of the theory of heterophase reactions of this kind.

Experimental studies on adsorption in direct syntheses of chlorosilanes and alkyl(aryl)chlorosilanes proved the validity of the mechanism involving the chemisorption of the organic chloride without dissociation of a single-atom active centre[103,128]; it has been shown[128] that the hypothesis of the dissociative adsorption of methyl chloride at two centres in the formation of dichlorodimethylsilane[1,21,86–88,93,129] is invalid. In the light of the foregoing one must assume that the active centre on the surface of the solid reactant in the direct synthesis includes silicon atoms, one (for R_2SiCl_2) or more (for $RSiCl_3$) valencies of which are bound to chlorine.

In all probability the reactions in the formation of dialkyl(aryl)chlorosilanes are accompanied by a rearrangement of the coordination sphere with transition of the reacting silicon atom to a state with an increased valence[106,130]. However, we believe that the available data are inadequate to infer unambiguously the composition of the intermediate complexes in the direct synthesis of alkyl(aryl)chlorosilanes. The mechanism of the formation of dialkyl(aryl)chlorosilanes, supported by experimental evidence, can be represented schematically as follows[99,106–108,114]:



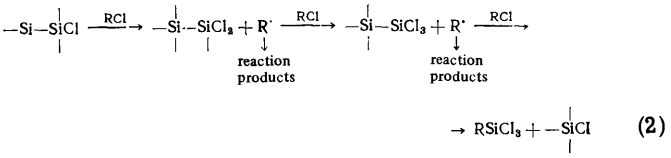
$$-\overset{|}{\underset{|}{Si}}-\overset{|}{\underset{|}{SiCl}} + 2RCl \rightarrow R_2SiCl_2 + -\overset{|}{Si}Cl \quad (1)$$

A similar mechanism was put forward in another study[130], where an attempt was made to elaborate it in greater detail in conjunction with the consideration of tentative intermediate stages, in particular the formation of the surface compounds $RSiCl_2$, etc. The approximate calculations carried out in that investigation confirmed that the formation of the dialkyl(aryl)chlorosilane molecule can be accompanied by the regeneration of the surface compound — the product of the partial chlorination of the silicon atom at the centre of a neighbouring tetrahedron.

The proposed mechanism reflects satisfactorily the experimental findings. The increased yields of dialkyl(aryl)chlorosilanes after the introduction into the reaction of optimum amounts of chlorine donors (HCl and CuCl), the acceleration of the formation of dialkyl(aryl)chlorosilanes in the initial stage of the reaction[131] after the generation of sufficient active centres, and the selective formation of R_2SiCl_2 under conditions where the decomposition processes take place at the minimum rate[7] (the increase of the degree of chlorination of silicon and chain termination in the formation of R_2SiCl_2 are relatively inhibited) can be understood.

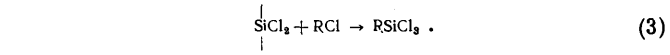
The formation of R_2SiCl_2 at advanced stages in the reaction involving silicon (i.e. as the solid reactant is deactivated) is known to be promoted by a gradual increase of temperature in the reaction zone[132]. The decomposition of the organic chloride is then accelerated. Under certain conditions, this leads to the formation of new active centres, the generation of new chains, and the restoration of the rate of formation of the dialkyl(aryl)chlorosilane.

It has been suggested[107,108] that the formation of alkyl(aryl)trichlorosilanes proceeds in all probability with chain propagation (in the absence of a catalyst):



$$\rightarrow RSiCl_3 + -\overset{|}{Si}Cl \quad (2)$$

or with chain termination (in a catalytic process).



$$\overset{|}{SiCl_3} + RCl \rightarrow RSiCl_3 . \quad (3)$$

Podgornyi et al.[133] adopted these mechanisms with an additional consideration of possible intermediate stages.

CH_3SiFCl_2, CH_3SiF_2Cl, and CH_3SiF_3 were evidently detected owing to these factors in the formation of trihalogenomethylsilanes by the reaction of methyl chloride with the surface of silicon treated with hydrogen fluoride[99]. Therefore in the synthesis of trichlorophenylsilane in the absence of a catalyst the introduction of hydrogen chloride (the reaction initiator) makes it possible to increase very sharply (by a factor greater than 10) the rate of formation of the required product[108]. The reaction begins with the interaction of hydrogen chloride involving the formation of $SiCl_n$ active centres. The latter can react with hydrogen chloride, forming trichlorosilane and silicon tetrachloride (their content in the mixture of products is usually about 35%) or the compounds $SiCl_n$ can enter into the composition of the active centres on which chlorobenzene decomposes with formation of more highly chlorinated products and adds

on with regeneration of the products of the partial chlorination of silicon. Thus the amount of consumed HCl corresponds to the amount of trichlorosilane and silicon tetrachloride formed.

In the presence of a catalyst the temperature of the synthesis of chlorophenylsilanes can be reduced by approximately 150 deg C. Then in the absence of hydrogen chloride the formation of the primary active centres involving the surface compounds $SiCl_n$ proceeds mainly in the catalytic decomposition of chlorobenzene and chlorination of silicon by the CuCl formed, which plays the role of an initiator. The additional introduction of relatively small amounts of hydrogen chloride results in this case too in an increase of the rate of the process and (to the greatest extent) of the rate of synthesis of dichlorodiphenylsilane (Fig. 1). With increase of the concentration of hydrogen chloride, the rate of formation and content of dichlorodiphenylsilane in the mixture of reaction products through a maximum. Under the conditions adopted, hydrogen chloride not only initiates the process but also behaves as a reactant in the formation of trichlorophenylsilane, which is illustrated by the sharp decrease of the fraction of products derived from phenyl radicals per mole of trichlorophenylsilane with increase of the amount of added hydrogen chloride[108]. The involvement of hydrogen chloride leads to an increase of the degree of chlorination of the surface compounds and evidently to chain termination. As a result, the overall rate of formation of chlorophenylsilanes falls (with increase of the fraction of trichlorophenylsilane in the reaction products).

When the reaction is carried out in the presence of solid reactants with a high catalytic activity, the overall rate of formation of chlorophenylsilanes in specific syntheses of dichlorophenylsilane is always higher, owing to the chain mechanism of its formation, than in processes with preferential formation of trichlorophenylsilane[20,108,134].

Alkyl(aryl)dichlorosilanes are always formed with participation of hydrogen chloride and the surface intermediates $HSiCl$.[7,53,99,128,135]. The experimental evidence for the mechanism of the process

$$\begin{matrix} H \\ -Si- \\ Cl \end{matrix} \xrightarrow{RCl} RSiHCl_2 \qquad (4)$$

is quite reliable. However, we believe that there is no justification for the total exclusion of chain reactions from this process (for example, with participation of the surface compounds $HSiCl_2$)[115].

The formation of trialkyl(aryl)chlorosilanes R_3SiCl, the products of the disproportionation of alkylation of R_2SiCl_2,[136,137] also involves the chlorination of silicon, which is responsible for the primary formation of R_2SiCl_2.

It is noteworthy that the above mechanisms of the interaction between the organic chloride and the solid reactant is simplified (in particular the role of the copper catalyst in the mechanisms is not taken into account) and do not reflect fully the complex process in which the formation of particular products of the partial chlorination of silicon and the nature of their subsequent interaction with the organic chloride (the intermediates can also interact) are influenced by a multiplicity of different factors.

2. The Role of the Catalyst. The Involvement of Copper in the Transfer of Chlorine from the Organic Chloride to Silicon

With increase of the R–Cl bond strength[138] in the series $C_3H_7Cl < C_2H_5Cl < CH_3Cl < CH_2 = CHCl < C_6H_5Cl$, the temperature of the direct synthesis of the corresponding alkyl(aryl)chlorosilanes rises[7,21,22]. This suggests that the activation of the organic chloride[7,53,85,106] is an important condition for the successful occurrence of the process. Copper is known to catalyse the reactions with organic chlorides[139] and has been used widely[140] also in direct syntheses.

The vast majority of the relevant publications deal with the methods of preparation and properties of the copper catalyst. In considering the role of copper in the direct synthesis of alkyl(aryl)chlorosilanes attention has been concentrated on the activation of silicon.

The activation of pure silicon is possible as a result of the change in the electronic state of the surface atoms ("the collective electronic effect") and the decrease of the Si–Si bond strength when microamounts of copper (about 10^{17} atoms cm^{-3}) are dissolved in it[111,128]. (Shiihara and Iyoda[141] was the first to draw attention to the dependence of the increase of the activity of silicon on the decrease of the Si–Si bond strength when copper, iron, aluminium, or calcium are present in its silicon lattice). However, this effect is characteristic not only of copper but also of certain other elements present in silicon[128,142]. This conclusion is confirmed by the higher reactivity of technical silicon, which usually contains about 2% of impurities, compared with pure silicon in all the direct synthesis investigated[31,48,86,104,113,143]. Therefore the practical importance of this effect of copper in the employment of technical silicon is small and copper does not stabilise the reactivity of various technical silicon specimens differing in their collective electronic properties in the initial state[128].

The increase of the reactivity of surface silicon atoms is more significant when chlorine atoms combine with them[37,106,130]. Surface compounds of the type $SiCl_n$ also behave as centres for the activation of the organic chloride[107].

The involvement of copper in the transfer of chlorine from the organic chloride to silicon via the mechanism

$$RCl + Cu \rightarrow CuCl + R^{\cdot} \text{ or its reaction products,} \qquad (5)$$

$$CuCl + Si \rightarrow \begin{matrix} | \\ -SiCl \\ | \end{matrix} + Cu \qquad (6)$$

was suggested in the first study of the mechanism of the direct synthesis of alkyl(aryl)chlorosilanes[11]. Many investigators who studied the direct synthesis subsequently reached the same conclusion[7,41,45–47,53,141]. Furthermore, it has been shown for the reaction with methyl chloride that the ability of copper to form copper(I) chloride determines to a large extent its activity in the direct synthesis of chloromethylsilanes[144]. An attempt has actually been made[45] to relate the decrease of the induction period in this process to the catalytic influence of the aluminium present in silicon on the formation of CuCl.

Assuming that the stage involving the transfer of chlorine to silicon with participation of CuCl is the most important link in the entire process, Japanese[141,145–150] and German[45–47,151–153] investigators made a detailed study of the reaction between copper(I) chloride and silicon. The temperatures of the onset of reaction[146,151,152] and many other kinetic characteristics[145,147–149] were determined and the different stages of the interaction[148,149,152]; the composition of the compounds formed[152], and the effect of various factors on the reaction[45,141,148–150] were studied.

Interesting data on the involvement of copper in chlorine transfer to silicon with formation of the $SiCl_n$ intermediates were obtained recently in a study of the direct synthesis by pulse gas chromatography[99,107]. When silicon was treated with chlorine, the main product of its subsequent reaction with methyl chloride was trichloromethylsilane[107].

The presence of copper in the silicon alloy was responsible for the formation of dichlorodimethylsilane in similar experiments[99]. Dichlorodimethylsilane was found to predominate also in the reaction of methyl chloride with silicon (in the absence of copper) treated with hydrogen chloride.

Under the conditions adopted, chloromethylsilanes are obtained almost wholly with participation of the $SiCl_n$ surface compounds formed beforehand. When chlorine is replaced by hydrogen chloride in the preliminary treatment of silicon, the species SiCl,[107] whose involvement in the reaction with methyl chloride leads to the formation of dialkyl(aryl)chlorosilanes as the main product, predominates among the $SiCl_n$ surface species instead of $SiCl_2$ and $SiCl_3$. The formation of dichlorodimethylsilane in the reaction with the silicon–copper alloy suggests that in the presence of copper the chlorination of silicon also leads to the preferential formation of SiCl. Thus copper involved in the chlorine transfer processes apparently influences the composition of the compounds $SiCl_n$, promoting the formation of the partial silicon chlorination products which are responsible for the synthesis of dialkyl(aryl)dichlorosilanes.

Therefore the introduction of copper(I) chloride into the reaction zone can increase significantly the content of dialkyldichlorosilanes in the mixture of products. The removal of CuCl from the solid reactant in the direct synthesis (by reducing it with hydrogen) leads to the disappearance of the dialkyldichlorosilane $[(C_2H_5)_2SiCl_2]$ from the reaction products[53,85]. The involvement of the copper catalyst in the transfer of chlorine to silicon probably constitutes an extremely important function of the catalyst in direct syntheses whose temperature is much lower than the temperature of the reaction between copper(I) chloride and silicon.

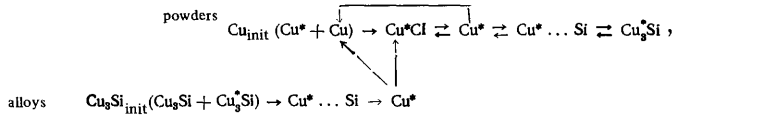
If the decomposition (dehydrochlorination) of the alkyl chloride proceeds at a temperature lower than that at which copper(I) chloride is reduced by silicon or the synthesis is carried out with introduction of hydrogen chloride from outside, the surface products of the partial chlorination of silicon are formed readily also without the involvement of copper (by the reaction between silicon and HCl) and the above function of the catalyst is not manifested. These data have been interpreted in some studies[21,104,111–113,128] as evidence for the rejection of the involvement of CuCl in all the processes of the direct synthesis.

Some investigators refer to the possibility of the synthesis, for example of chloroisopropylsilanes (in which the compounds $SiCl_n$ and HSiCl are formed by the reaction of silicon with hydrogen chloride, produced by the dehydrochlorination of isopropyl chloride) at 110–120°C, while CuCl is reduced by silicon under analogous conditions only at 260°C.[21] Others motivate their objections by the fact that the CuCl introduced from outside did not accelerate the reaction with hydrogen chloride in their experiments[104]. However, under these conditions an acceleration of the reaction was not in fact to be expected, since the synthesis occurred, according to the data of the above investigators themselves, at temperatures (230° and 220°C for the purified and technical silicon respectively[104]) lower than that of the reaction of CuCl with silicon (269° and 234°C for the same silicon specimens[113]). This applies also to the introduction of copper(I) bromide (the temperature of its reduction by silicon is 300°C[112]) in the reaction between hydrogen bromide and silicon (reaction temperature 220°C[110]).

When pure silicon (99.9999%) is used, the temperature of the synthesis of trichlorosilane and dichloromethylsilane (from methyl chloride and hydrogen chloride) increases to 320°C.[104,111]. Therefore it is quite understandable why in the presence of CuCl these products are formed at a temperature as low as 260–280°C,[111] which corresponds according to the author's data, to the temperature of the reduction of CuCl by pure silicon (279°C)[113].

In the synthesis of alkyl(aryl)chlorosilanes (R = CH_3, C_2H_5, or C_6H_5) the introduction of CuCl as a rule activates the reactions[7,53,116] and CuCl is directly involved in the formation of the required product[53,85]. However, the role of CuCl in the direct synthesis of alkyl(aryl)chlorosilanes is apparently not limited to the transfer of chlorine from the organic chloride to silicon. The prolonged activity of the copper catalyst observed in the processes can be accounted for by the high catalytic activity of the copper itself, which is continually formed as a result of the reduction of copper(I) chloride[116]. The activity of the copper catalyst obtained by the reduction of CuCl by silicon has been demonstrated in the synthesis of chloromethylsilanes[21,154]. In particular, at a temperature as low as 250–300°C this copper forms with silicon the intermetallic compound Cu_3Si, while in the presence of crystalline copper, which is relatively inactive in the synthesis, Cu_3Si is obtained only at temperatures above 1000°C.[144]

Generallising from the literature data, the involvement of copper in the synthesis can be represented by a series of complex reversible phase transformations which the most active fraction of the initial copper or Cu_3Si gives rise to CuCl, which is reduced by silicon with formation of unstable catalytically active copper, the intermediate Si–Cu compounds, and ultimately intermetallic phases, including Cu_3Si:[116,117,131]



where an asterisk denotes an active form of copper and Cu is crystalline copper with a low activity.

The activity and the necessary concentration of the initial copper in the reaction zone depend markedly on its properties (for example, the proportion of structural defects) and the conditions in the formation of CuCl [in particular the energetics of reaction (5)][117]. An increased proportion of structural defects can be achieved by mechanical treatment of the powders (copper flakes) or by rapid cooling of silicon–copper alloys[155]. Reaction (5) becomes more favourable on energy grounds, particularly after the addition of promoting additives–Group II elements (see subsection 3 of the present Section).

All this promotes a sharp increase of activity and at the same time a decrease of the optimum catalyst concentration[6]. Possibly not all the copper in the reaction zone catalyses the direct synthesis: the active form of copper is responsible for catalysis. If the entire copper introduced were involved in the process, then in the course of the phase transformation the reactivity of the solid reactants having the same chemical composition would ultimately reach the same level, which is inconsistent with experimental data. Experiment shows that, in order to attain satisfactory rates the selectivities in the synthesis of alkyl(aryl)chlorosilanes in the presence of highly active copper, a very low content of the latter in the solid reactant is sufficient[53,156]. However, under inductrial conditions it is as a rule necessary to employ higher copper concentrations, since during the process part of the copper may be deactivated by harmful impurities in the reactants and by side products and can also undergo recrystallisation[53,157,158]. Therefore, in order to utilise the silicon as fully as possible, it is frequently desirable to introduce the required amount of catalyst gradually in the course of the synthesis and not all at once. This makes it possible to reduce the rates of the

undesirable decomposition reactions of the organic chloride under the influence of the organic chloride under the influence of the excess amounts of copper.

The weakening and dissociation of the C–Cl bond and the formation of CuCl apparently constitute a slower stage than the transfer of chlorine from copper to silicon[116]. Therefore in the direct synthesis of alkylchlorosilanes (280 to 370°C) the steady-state concentrations of copper(I) chloride determined in the solid reactant under experimental conditions are much higher (up to 8%)[85] than in the synthesis of chlorophenylsilanes (at most about 1%)[131], where the formation of CuCl is hindered by the increased strength of the bond between chlorine and the phenyl group[138], the interaction of chlorine with silicon being accelerated at a high temperature in the reaction zone (450°C)[159,160].

Possibly the intermediate CuCl determined in the solid reactants removed from the reactor during the direct synthesis does not constitute an independent phase, but is bound chemically to the solid reactant in the form of a surface compound[21,46]. It is also likely that the product of the reaction of the organic chloride with copper in the solid reactant is more reactive than ordinary CuCl and reacts with silicon at a lower temperature, particularly since ordinary CuCl exists in a polymeric form[161–163].

The composition of the admixtures in silicon greatly influences its reactivity (the temperature of the onset of reaction) in the interaction with CuCl[113,141] and the composition of the compounds formed from CuCl and silicon or from HCl and silicon in the presence of copper[141]. The influence of various elements in the solid reactants on the direct synthesis of chloromethylsilanes[164–169], chloroethylsilanes[143], and chlorophenylsilanes[170], which is known and has been frequently discussed, is in many respects determined by their influence on the formation of surface compounds of the type $SiCl_n$ (in particular from CuCl and silicon), which play a most important role throughout the process.

Intermetallic compounds of copper and silicon, including Cu_3Si (the so called η-phase) evidently serve as a source of the formation and renewal of the catalytically active copper, but it has been established[171] that Cu_3Si does not play the exceptional role which was attributed to it in some investigations[1,21,86,93,129,154,172]. (The activity of the intermetallic phases obtained in the reduction of CuCl by silicon is higher than that of the alloy phases[131,144]).

The intermediate surface compounds of silicon and copper, in the silicon atoms of which electronic changes associated with the local effect of copper (the "local electronic effect") take place, are apparently important for the catalysis of the synthesis of alkyl(aryl)chlorosilanes (without the involvement of hydrogen chloride), in particular of the selective formation of dialkyl(aryl)dichlorosilanes[128]. However, the author does not explain in what way the local effect of copper facilitates the formation of dialkyl(aryl)dichlorosilanes.

3. The Involvement of Promoting Agents in the Transfer of Chlorine from the Organic Chloride to Copper and Silicon.

Analysis of the literature shows that the introduction of promoting additives is the most effective means of increasing the overall activity and of controlling the selectivity of the solid reactants in the direct synthesis. Elements of all the Groups in the Periodic System (and combinations of compounds of these elements), other than those of Groups VI and VII, have been recommended in numerous publications[143,165,166,173–186].

The majority of promoting agents have been discovered empirically and they influence one of the parameters of one or two similar processes. Thus antimony and bismuth activate the synthesis of chloromethylsilanes[31,181] and chloroethylsilanes[53], but do not affect the formation of chlorophenylsilanes[170], while sodium compounds added in the preparation of chloromethylsilanes[179] deactivate the solid reactants in the synthesis of chlorophenylsilanes[170]. Calcium and its compounds promote the preferential formation of hydrogen-containing dichloroethylsilane[143], associated with the dehydrochlorination of ethyl chloride[135], while in the synthesis of chlorophenylsilanes they increase the yield of chlorotriphenylsilanes[170], which is formed without the involvement of hydrogen chloride.

The attempts to explain the mechanism of the effect of certain additives to silicon–copper alloys in the synthesis of chloromethylsilanes[169,187] were not continued, since the proposed explanations are difficult to reconcile with the hypotheses concerning the mechanism of the direct synthesis.

Some investigators[116,117,188] put forward the idea that very effective promoting agents for various direct syntheses, particularly those involving the selective formation of dialkyl(aryl)dichlorosilanes (zinc, cadmium, and their compounds), participate in the transfer of chlorine from the organic chloride to copper and silicon via reactions (5) and (6). The experimental data are in good agreement with this hypothesis.

In the synthesis of chlorophenylsilanes in the presence of the most active promoting agents (cadmium compounds) the solid reactants contain as a rule not less than 1% CuCl, the solid reactants with less active promoting agents (zinc compounds) contain about 0.5% CuCl, while in the absence of promoting agents the CuCl content does not exceed the error of its determination (± 0.05%)[131].

The involvement of CuCl in the phase transformations of the solid reactant is accompanied by the formation of Cu_3Si (Krylov et al.[144]) (see also the scheme on p. 218. Therefore the relative content of Cu_3Si in the solid reactant can serve by convention as a measure of the involvement of CuCl in the process. When a mixture of silicon and copper powders is heated in the presence of promoting agents ($ZnCl_2$, $CdCl_2$) in an atmosphere of nitrogen at 450°C, the intermetallic compound Cu_3Si is formed (up to 70% of the total amount of copper). In analogous experiments without promoting agents Cu_3Si is not formed[116,131].

We believe that the change in the reactivity of the solid reactants (with and without promoting agents) during the synthesis of chlorophenylsilanes and the correlation between the relative content of Cu_3Si in the solid reactants and their reactivity (Fig. 3) also indicate an effect by the promoting agents on the chlorine transfer processes, which determine the course of the synthesis[131]. This is apparently of greatest significance in the initial most important period in the formation of the active form of the catalyst with participation of CuCl. By being involved in the formation of CuCl, the promoting agents thereby influence the phase transformations as a whole. The latter has an appreciable effect on the synthesis.

The fact that the presence of promoting agents in the solid reactant affects significantly the influence of the active source of chlorine (hydrogen chloride) introduced into the reaction zone (Fig. 4) constitutes yet another confirmation of the hypothesis that promoting agents influence the chlorine transfer processes. Fig. 4 shows that in the synthesis using a solid reactant without promoting agents the introduction of HCl can accelerate the formation of chlorophenylsilanes by a factor of 3.5, in the presence of zinc

only by a factor of 2, and in the presence of cadmium or a cadmium-zinc mixture the rate remains constant or falls[116].

Evidently the promoting agents involved in chlorine transfer facilitate the latter. It has been shown[108] that the characteristics of the reactions occurring when both promoting agents and HCl are introduced agree well with the chain mechanism of the direct synthesis.

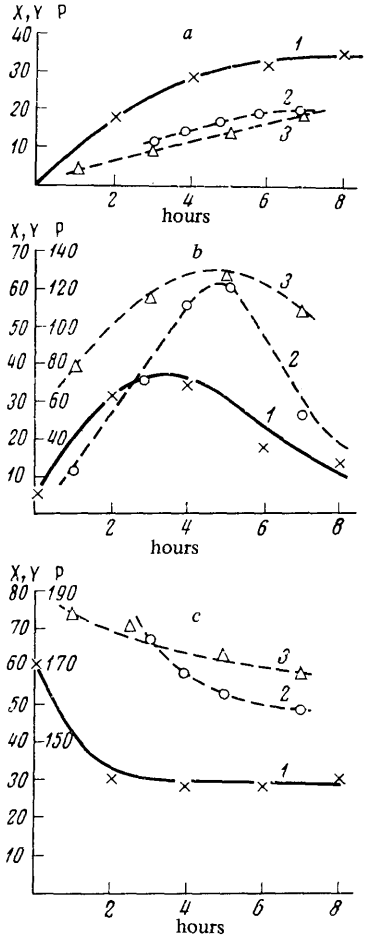


Figure 3. Phase composition of the solid reactants (curves *1*), their overall reactivity in the synthesis of chlorophenylsilanes (curves *2*), and their selectivity in the formation of dichlorodiphenylsilane (curves *3*): *a*) for a silicon–copper composition; *b*) for a silicon–copper–zinc oxide composition; *c*) for a silicon–copper–cadmium chloride composition; *X* = copper contained in Cu_3Si (per cent of total copper); *Y* = dichlorodiphenylsilane content in the mixture of reaction products (%); *P* = rate of formation of chlorophenylsilanes in the presence of 1 kg of solid reactant (g h^{-1}); the time from the start of synthesis is plotted as abscissa.

The involvement of promoting agents in chlorine transfer is also manifested in their influence on the synthesis of chlorophenylsilanes when another chlorine donor (trichlorosilane) is introduced[114]. The rate and selective reactivity in the direct synthesis of alkyl(aryl)chlorosilanes are to a large extent determined by the concentration and composition of the surface compounds $SiCl_n$. The effect of trichlorosilane reduces virtually to the involvement of the silyl radical $SiCl_3^{\cdot}$ in the process.

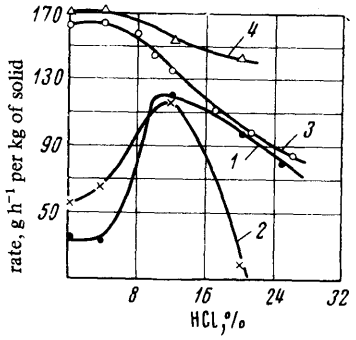


Figure 4. Effect of hydrogen chloride on the synthesis of chlorophenylsilanes in the presence of different solid reactants: *1*) without promoting agents; *2*) with zinc oxide; *3*) with cadmium chloride and zinc oxide; *4*) with cadmium chloride; the percentage of HCl in the mixture with chlorobenzene is plotted as abscissa.

In the absence of promoting agents, when the transfer of chlorine from chlorobenzene to silicon is relatively difficult, the introduction of trichlorosilane in all probability results in further formation of the compounds $SiCl_n$, corresponding to different degrees of chlorination, via the mechanism

$$-\overset{|}{\underset{|}{Si}}- \xrightarrow{SiCl_3^{\cdot}} -\overset{Cl}{\underset{|}{Si}}- + SiCl_{2\,ads} \cdot \qquad (7)$$

This results in an increase of the rate of formation of $C_6H_5SiCl_3$ and, what is most interesting, of $(C_6H_5)SiCl_2$ (Fig. 5). Fig. 5 shows that in the presence of $CdCl_2$ the rate of formation of $(C_6H_5)_2SiCl_2$ falls and the rate of formation of $C_6H_5Cl_3$ increases. This is consistent with the hypothesis that the presence of $CdCl_2$ has a favourable effect on the formation of the surface compounds SiCl via the mechanism

$$-\overset{|}{\underset{|}{Si}}- \xrightarrow[Cu,CdCl_2]{C_6H_5Cl} -\overset{Cl}{\underset{|}{Si}}- + \underset{\text{reaction products}}{C_6H_5^{\cdot}} \cdot \qquad (8)$$

In this case the involvement of the silyl radical apparently leads to an increase of the degree of chlorination via the mechanism

$$-\overset{Cl}{\underset{|}{Si}}- \xrightarrow{SiCl_3^{\cdot}} -\overset{Cl}{\underset{Cl}{Si}}- + SiCl_{2\,ads} \qquad (9)$$

and the formation of surface compounds which determine the synthesis of alkyl(aryl)trichlorosilanes. In conformity with these mechanisms, the formation of $C_6H_5SiCl_3$ with participation of trichlorosilane and in the absence of promoting agents is not accompanied by the liberation of the reaction products obtained from the phenyl radical:

$$SiCl_{2\,ads} + C_6H_5Cl \rightarrow C_6H_5SiCl_3 \cdot \qquad (10)$$

In the presence of $CdCl_2$ one mole of products from the phenyl radical is formed per mole of $C_6H_5SiCl_3$, which probably corresponds to the initial formation of SiCl with participation of chlorobenzene via mechanism (8).

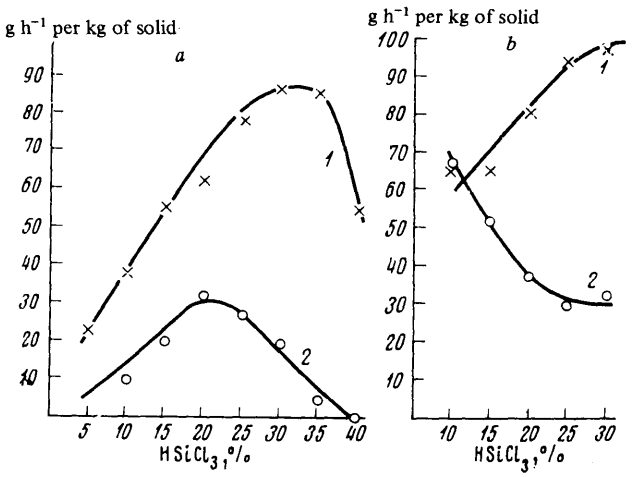


Figure 5. Rates of formation of trichlorophenylsilane (curves *1*) and dichlorodiphenylsilane (curves *2*) in synthesis in the presence of trichlorosilane; *a*) involving a silicon–copper reactant; *b*) involving a solid reactant with added cadmium chloride.

In their explanation of the mechanism of the action of promoting agents on chlorine transfer processes in the direct syntheses some investigators[116,117,188] began with the postulate that the transfer of chlorine to copper is appreciably hindered owing to the comparatively high strength of the bonds between the copper atoms in the crystal lattice, which can reach 81.1 kcal mole^{-1} (Skinner[8]) (in particular for powdered copper). It therefore appears useful to replace the single-stage formation of CuCl via reaction (5) by an energetically more favourable two-stage process, for example via the mechanism

$$RCl + M \rightarrow MCl + R^{\cdot}, \quad (11)$$
$$MCl + Cu \rightarrow CuCl + M. \quad (12)$$

Here the metal M must satisfy the following requirements: (a) it must be relatively readily atomised or must have a lower heat of sublimation than copper; (b) it must have a relatively high affinity for chlorine, which does not, however, exceed the chlorine–copper bond strength. These requirements are met, in particular, by Group II metals (zinc and cadmium), which, as already stated, are the most common and effective promoting agents in the direct synthesis[134,189–203]. Approximate calculations in the above studies showed that the formation of CuCl by reactions (11) and (12) with participation of promoting metals (including the processes where zinc or cadmium oxides or chlorides are introduced into the solid reactants) is preferred on energy grounds.

In the synthesis or chloromethylsilanes the use of the above promoting agents in combination with other procedures made it possible to achieve a virtually selective synthesis of the most valuable monomer, $(CH_3)_2SiCl_2$, the values of other reaction parameters being high. In the synthesis of chloroethylsilanes the content of $(C_2H_5)_2SiCl_2$ reaches 70 to 80% of the weight of the compounds formed[6].

Compared with the synthesis of chloromethylsilanes and chloroethylsilanes, the synthesis of chlorophenylsilanes at a high rate with the selective formation of $(C_6H_5)_2SiCl_2$ is most difficult, because the transfer of chlorine to copper and silicon is additionally hindered by the greater strength of the C–Cl bond in chlorobenzene[138] and the solid reactants consist of powdered mixtures instead of alloys[131]. For this reason the effect of the above Group II elements is particularly marked in this process[6,204] (see Table).

Effect of zinc, cadmium, and their compounds on the synthesis of chlorophenylsilanes.

Promoting agent	Rate of formation of mixture of chlorophenylsilanes, g h^{-1} per kg of solid reactant	Contents in mixture of reaction products, %			
		C_6H_5	$C_6H_5SiCl_3$	$(C_6H_5)_2$	$(C_6H_5)_2SiCl_2$
None	30–35	13–30	32–43	12–23	16–20
Zn or its compounds	50–80	14–17	26–32	2–3	45–50
Cd or its compounds	120–170	4–7	26–32	7–11	47–60
Mixture of Zn and Cd or their compounds*	150–200	2–7	4–15	0.3–1.0	70–80

* When combined promoting agents are used, the content of $(C_6H_5)_3SiCl$ in the reaction products reaches 5–9%.

The use of zinc and cadmium compounds as promoting agents made it possible for the first time to achieve more complex direct syntheses of organosilicon derivatives of heterocyclic compounds[202] and also of alkyl(aryl)chlorosilanes containing Si–C–Si linkages[203] with quite satisfactory results.

The regulation of the chlorine transfer processes and of the formation of the $SiCl_n$ surface intermediates by the introduction of promoting agents into the solid reactant and of chlorine donors into the gas phase made it possible to devise different versions of specific industrial synthesis[6].

The involvement of promoting agents in the chlorine transfer processes does not rule out the possibility of their influence on other stages of the process, in particular on the formation of the catalyst Si–C bond[116]. However, their effect on the chlorine transfer stage evidently plays a major role, because this state to a large extent determines the course of the entire direct synthesis.

Many important practical problems have been solved successfully on the basis of the ideas discussed above, whose development involved a major contribution by S. A. Golubtsov. This can serve as one of the criteria for the assessment of their validity and importance.

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Advances in the Chemistry or Organosilicon Polymers

V.V.Korshak and A.A.Zhdanov

The great synthetic possibilities in the chemistry of organosilicon systems and the wide variety of their properties are discussed. The high reactivity of cyclic organosilicon systems with respect to various rearrangements and polymerisation, which gives rise to unlimited possibilities for the synthesis of macromolecular organic derivatives of the elements, is specially considered. The bibliography includes 222 references.

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I. INTRODUCTION

In view of the successful development of the chemistry of organic polymers, chemists during the first half of the 20th century had great expectations, and not without justification, from silicon as the closest analogue of carbon. However, a more detailed investigation of the chemistry of organosilicon compounds showed that silicon is incapable of forming very long polymeric chains made up of carbon atoms (analogous to polymeric carbon chains). The idea of the formation of a polymeric chain from alternating silicon and oxygen atoms led to the discovery of a new class of high-molecular-weight compounds—polymers with inorganic principal molecular chains.

K.A.Andrianov played a leading role in formulating and developing this new field of polymer chemistry. This branch of chemistry reached the greatest development in his studies and those of his numerous students.

The development of the chemistry of organosilicon polymers began in 1937 in a study by Andrianov[1] where the possibility of the formation of polymer chains from alternating silicon and oxygen atoms was demonstrated[1,2].

The research by Andrianov's school is distinguished by an exceptionally wide range of studies and by the practical applications of most of them. The investigations by Andrianov and his students laid the foundations of the chemistry of polymeric organic derivatives of the elements, which led to the discovery of the class of thermostable polymers.

Polyorganosiloxanes were the first polymers meeting the more rigorous requirements of many branches of modern engineering. These polymers have a high thermal stability and a high resistance to moisture, are chemically inert, and resist the action of sunlight, oxygen, and ozone. The chemical compositions and structures of compounds of this class are responsible for their valuable technical properties.

In terms of structure, polyorganosiloxanes occupy an intermediate position between organic polymers and silicate structures. This class of polymers has no analogues in nature as regards composition and constitutes a truly synthetic class.

Andrianov's research in the field of polyorganosiloxanes enabled him to formulate and apply in subsequent investigations the principle of combining in the polymer chain elements with appreciably different electronegativities. This idea has been reflected in a number of Andrianov's studies in the field of polyorganosiloxanes derivatives of the elements.

During the last 15 years Andrianov carried out fundamental research in the field of non-traditional and specific structures of polymeric molecules (cyclonetwork, cyclolinear, ladder, spirocyclic, etc.) in addition to studies on the classical structures of organosilicon polymers (linear and branched). The fundamental principles of the formation of the siloxane chain as well as the chemical and physical properties of polymers of the polyorganosiloxane series have been described in a number of monographs[3-6] embracing the literature data up to 1964. The main practical applications of substances of this class have been described in other monographs[7-16]. The aim of the present review was to examine studies carried out in recent years by the Soviet School of Chemists working in the field of organic silicon chemistry and headed by Andrianov.

II. LINEAR AND BRANCHED POLYORGANOSILOXANES

The polymerisation reactions of cyclic organosilicon compounds have now acquired great theoretical and practical interest, since they provide one of the most important ways of synthesising oligomers and high-molecular-weight compounds with inorganic and organic-inorganic molecular chains[4,5]. The vast majority of initiators employed consist of compounds whose molecules contain one nucleophilic centre (for example, OH^-, $\rangle NH_2^-$, or R_3SiO^-).

Andrianov and coworkers developed methods for synthesising many-centre initiators[17]. Three-centre initiators were obtained via the scheme

$$RSiCl_3 + 3NaOSi(CH_3)_2OSi(CH_3)_2ONa \rightarrow RSi[OSi(CH_3)_2OSi(CH_3)_2ONa]_3,$$

where R = CH_3, C_2H_5, or C_6H_5. Four-centre initiators were prepared by a similar reaction:

$$SiCl_4 + 4\,NaOSi(CH_3)_2OSi(CH_3)_2ONa \rightarrow Si[OSi(CH_3)_2OSi(CH_3)_2ONa]_4 .$$

Polymerisation in the presence of many-centre initiators made it possible [17-19] to obtain high-molecular-weight polymers having a branched star-shaped molecular structure:

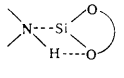
$$Si[OSi(CH_3)_2OSi(CH_3)_2ONa]_4 + n/4\,[(CH_3)_2SiO]_4 \rightarrow$$
$$\rightarrow Na[OSi(CH_3)_2]_lOSi(CH_3)_2OSi(CH_3)_2O\diagdown\!\diagup Si \diagup\!\diagdown OSi(CH_3)_2OSi(CH_3)_2O[Si(CH_3)_2O]_lONa \rightarrow$$
$$\rightarrow Na[OSi(CH_3)_2]_kOSi(CH_3)_2OSi(CH_3)_2O \diagup \quad \diagdown OSi(CH_3)_2OSi(CH_3)_2O[Si(CH_3)_2O]_mONa ,$$
$$l + k + l + m = n .$$

It was established that the order of the polymerisation reaction remains constant (it is first order with respect to the monomer) with increase of the number of functional groups in the initiators from 1 to 4. When two-centre initiators are employed, there is no interaction between the terminal functional groups and polymerisation proceeds independently via both reaction centres. With increase of the number of functional groups in the catalysts, there is a gradual decrease of the rate of polymerisation owing to the resulting steric hindrance due to adjacent side chains. The determination of the average number of branching centres by Kirby's method (from viscometric and light scattering data) showed that the branching of the molecules corresponds to the structure of the initial initiator [20,21]. The polydispersity coefficient of the polymers obtained amounts to 1.89–2.90, which indicates the occurrence of interchain exchange and chain transfer reactions at high conversions of the initial cyclic monomer [21].

It is interesting that the polymerisation of trimethyltriphenylcyclotrisiloxane in the presence of branched initiators does not lead to the formation of polymers with a star-like structure [22].

Studies on the type of change in the molecular weight distribution on polymerisation of various organocyclosiloxanes established that the polymerisation of octamethylcyclotetrasiloxane in the presence of NaOH involves chain transfer processes and the resulting polymer exhibits a high tendency towards depolymerisation. In the polymerisation of the same monomer in the presence of the initiator $(CH_3)_3SiON(CH_3)_4$ (with its subsequent elimination from the reaction sphere) a polymer is formed and secondary processes (chain transfer, branching) are not observed [23,24]. When the initiator is not removed, heating of the polymer *in vacuo* from 50° to 360°C leads in this case to depolymerisation with subsequent branching of the macromolecules.

The ideas on the mechanism of the anionic polymerisation of organosiloxane rings are based on the hypothesis of the formation of complexes between organocyclosiloxanes and nucleophilic agents [4]. A series of studies [25-30] undertaken to test this hypothesis established that molecular complexes are formed between amines and cyclosiloxanes [26-28]. The lifetimes of these complexes were established by NMR and it was found that the complexes are of a type different from that postulated previously. An experimental test of the possibility of the existence of complexes of the type NH...O$\begin{matrix}\diagup Si\\ \diagdown Si\end{matrix}$ showed [29] that the formation of a complex involving bonding of this kind is unlikely. The available data suggested a quasicyclic structure for the complexes with a non-linear hydrogen bond of the type



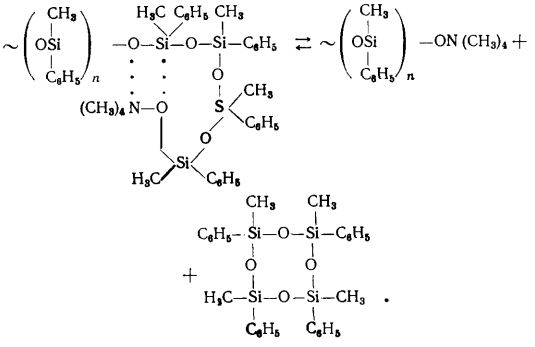
Furthermore, it was established that in the case of amines, in the absence of spectroscopically detectable admixtures of water, initiation begins with a direct attack on a ring silicon atom by the nitrogen atom [26,27].

A special series of studies in recent years was devoted to the investigation of polyorganosiloxanes containing phenyl groups at the silicon atom. Earlier investigations demonstrated an enhanced thermal stability of compounds of this class [31-33].

A study of the polymerisation of *cis*-trimethyltriphenylcyclotrisiloxane established that, owing to the high reactivity of the initial compound, the polymerisation reaction

$$[CH_3(C_6H_5)SiO]_3 + (CH_3)_4NO\left(\begin{matrix}CH_3\\|\\Si{-}O\\|\\C_6H_5\end{matrix}\right)_n{-}H \rightleftarrows (CH_3)_4NO\left(\begin{matrix}CH_3\\|\\SiO\\|\\C_6H_5\end{matrix}\right)_{n+3}{-}H \ldots$$

proceeds at a high rate. The depolymerisation reaction, leading to the formation of eight-membered and higher methylphenylcyclosiloxanes, proceeds at a relatively low rate and becomes appreciable only at high conversions [34-36]:

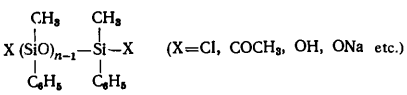


The polymerisation of *cis*-methylphenylcyclotrisiloxane in bulk, in the solid phase, and in solution leads to the formation of polymers whose actual molecular weight is appreciably lower than the molecular weight calculated from the ratio of the initiator and the cyclic compound. This can be accounted for by chain transfer reactions, traces of water and alcohols acting as chain-transfer agents. A preliminary removal from the reaction sphere of the possible chain-transfer agents leads to an increase of the rate of reaction almost by an order of magnitude and to a significant increase of the molecular weight of the resulting polymer [36].

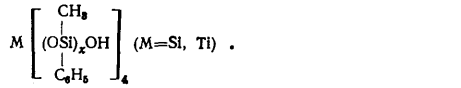
The highest yield of the polymer (95–98%) is achieved in the heterophase polymerisation of *cis*-trimethyltriphenylcyclotrisiloxane in hexane, which readily dissolves the initial cyclic compound but not the resulting polymer [37]. Side reactions, which usually lead to a broadening of the molecular weight distribution, are ruled out in this method and the polymer formed has an exceptionally low polydispersity coefficient ($M_w/M_n = 1.04$). Thermomechanical studies and studies on the hydrodynamic properties of polymethylphenylsiloxane showed that its chains are more rigid than those of polydimethylsiloxane [22].

One of the most promising procedures, which gives rise to great possibilities for controlling the composition and properties of polymers, involves the synthesis and study of linear and branched oligomers capable of conversion as a result of polymerisation and polycondensation into high-molecular-weight compounds with specified technical properties. A very important feature is that the polymerisation and polycondensation processes can be carried out directly in the finished articles.

The preparative methods devised hitherto make it possible to obtain oligomeric methylphenylsiloxanes having a wide range of terminal groups with different compositions [38,39].



The reactions of such oligomers with monomeric tetrafunctional compounds lead to the formation of oligomeric cross-like compounds with functional groups at the ends of the branches:

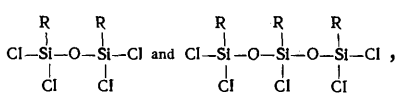


Both linear and cross-like oligomers, containing hydroxy-groups at the ends of the branches, are capable of further polycondensation. Polymers with $M = 10\,000$ and a glass point of 35°C can be obtained from linear oligomers [40]. The condensation of cross-like oligomers proceeds via both intermolecular and intramolecular mechanisms with formation of products having complex cyclic structures [41].

The glass points of linear oligomers decrease with increase of the molecular weight, while in the case of the cross-like oligomers they depend little on the lengths of the side chain but do vary significantly as a function of the nature of the terminal functional groups [42].

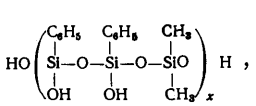
Cross oligomers with terminal hydroxyls exhibit the greatest resistance to thermo-oxidation, since on heating they form three-dimensional structures [43]. The replacement of the central silicon atom by titanium increases the thermal stability. Branched cross-like oligomers containing a certain amount of γ-trifluoropropyl groups show the greatest lubricating capacity [43].

Together with the methods of synthesis of siloxane oligomers described above, the hydrolytic condensation method merits a more detailed study, since the syntheses of the majority of organosilicon polymers are based on hydrolytic condensation processes and on the condensation of alkyl(aryl)chlorosilanes with different numbers of functional groups. The method of hydrolytic condensation in the vapour phase developed by Andrianov and coworkers [44,45] makes it possible to obtain organochloropolysiloxanes having the composition



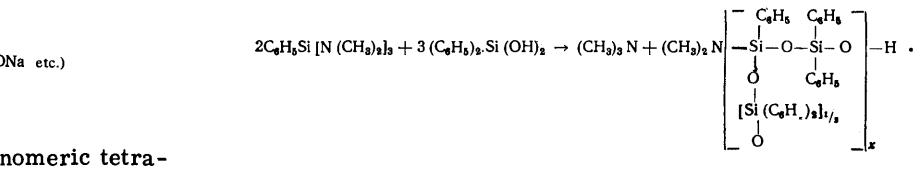
where R = C_6H_5 or C_2H_5.

The cohydrolysis of these compounds with dialkyl(aryl)-dichlorosilanes [44,46] yields oligomeric products having the composition

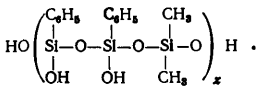


which were used to investigate the characteristics of three-dimensional polycondensation. It was established that the degree of reaction at the gel formation point and the critical branching coefficients exceed by a factor of 1.5–2 the values calculated by Flory's statistical theory. The explanation is that the condensation of the cohydrolysis products proceeds with a decrease of the number of functional groups owing to the formation of cyclic structures in the polymer units.

A similar feature was observed [44] in the condensation of aminosilanes and hydroxysilanes via the mechanism

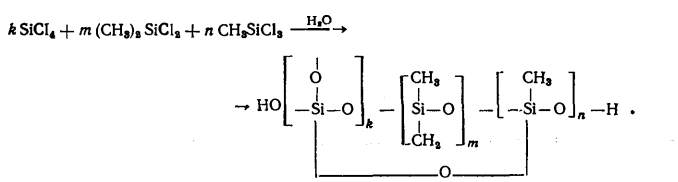


In this case the degree of reaction exceeds 90% but the resulting polymer is soluble and thermoplastic. Coatings with an appreciable resistance to petrol and oil were obtained [47] on the basis of the polyphenyldimethylphenylsiloxane oligomers investigated, which had the general formula



A study of polyfunctional systems, i.e. systems where the average number of functional groups in the initial monomers is greater than three, is of considerable interest. In such systems the C/Si ratio is appreciably reduced, which should lead to an enhancement of their thermal stability. Products of the cohydrolysis of silicon tetrachloride with dichlorodimethylsilane and chlorotrimethylsilane can serve as examples of such systems [48,49].

It was established that the yield of the gel fraction as a function of the number of functional groups in the initial system can be expressed by a polynomial equation [48], the yield of insoluble products depending also (separately) on the number of functional groups in the chlorosilanes employed. When appropriate hydrolysis conditions have been chosen, the above systems can give rise to soluble products despite the large number of functional groups in the system:



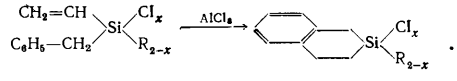
Oligomers with the above composition form protective coatings on metals, glass, and other materials. However, properties suitable for practical applications are achieved only when the average number of functional groups in the initial system is reduced to 2.6. [42]

The properties of polyorganosiloxane oligomers can be effectively modified by changing the nature of the organic group at the silicon atom as well as the number of functional groups in the initial monomers. The use of alkyl-(aryl)halogenosilanes containing 6–10 carbon atoms in the organic group attached to silicon in hydrolytic condensation reactions yielded compounds having the general formula $[RSiO(OH)]_n$, where $n = 6$ or 8 and R = i-C_5H_9, C_6H_{13}, C_8H_{17}, or C_9H_{19}. [50] These compounds condense in steps via an intramolecular mechanism. The cohydrolysis of higher alkyltrichlorosilanes with chloromethylsilanes and chlorophenylsilanes involves intramolecular condensation at a temperature not less than 60–65°C. [51] At lower temperatures each compound is hydrolysed separately.

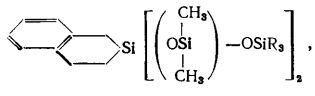
The cohydrolysis products are viscous transparent liquids, which polymerise in the presence of nucleophilic

agents. The methods devised for the synthesis of polyalkylsiloxanes served as the basis of a procedure whereby one can synthesise organosilicon liquids of new types with improved lubricating properties [52]. It was established that the introduction of units containing higher aliphatic groups at the silicon atom into polyorganosiloxane varnishes eliminates the formation of pores and bubbles when the varnishes dry out in thick layers [53].

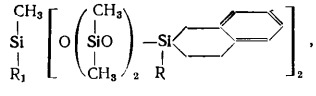
The modification of the properties of organosiloxane oligomers by altering the nature of the organic group at the silicon atom was continued in a series of studies by Andrianov on the synthesis and properties of compounds with arylalkyl groups at the silicon atom. The method of synthesis of compounds with arylalkyl groups at the silicon atom of the type $(C_6H_5CH_2CH_2)_xSiCl_{4-x}$ by the addition of chlorovinylsilanes to aromatic hydrocarbons, which was developed previously [54,55], served as the basis for the synthesis of bicyclic compounds via an intramolecular alkylation reaction [56-58]:



The introduction of silicon atoms with attached bicyclic fragments either into the siloxane chain or as blocking groups at the end of the chain yielded oligomeric products having the composition [59,60]

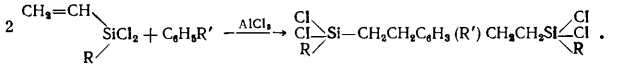


where R = CH_3, C_2H_5, or C_6H_5, or



where $R_1 = C_2H_4C_6H_4Cl$, which exhibit effective lubricating properties at high temperatures and retain them when used for a long time.

The viscosity of these compounds varies sharply with temperature and the activation energy for their viscous flow is high. Compounds suitable as high-temperature lubricants without these disadvantages were obtained by the above reaction [54,55], whereby one can also synthesise products of double intermolecular alkylation [60-62]:



Similar compounds were obtained also on the basis of compounds with two aromatic rings (diphenyl ether, diphenylmethane, biphenyl) [61]. In this case both silicon atoms add to the same aromatic ring via ethyl bridges:

$$[(CH_3)ClSiC_2H_4]_2C_6H_3—X—C_6H_5,$$

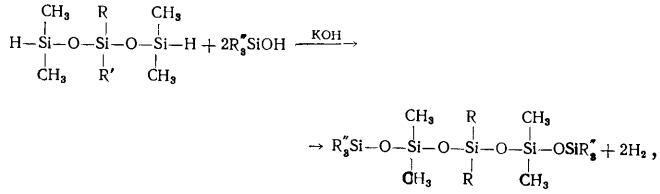
where X = CH_2 or O.

The replacement of chlorine atoms in the above compounds by trialkyl(aryl)siloxy-groups [60] yields the compounds

$$RC_6H_3\{C_2H_4SiR'_n[OSi(C_2H_5)_3]_{3-n}\}_2,$$

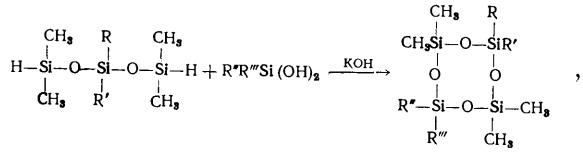
where R = H, CH_3, Cl, C_6H_5O, C_6H_5, or $C_6H_5CH_2$. They were used as the basis for high-temperature lubricants [63].

Together with hydrolytic condensation, the dehydrocondensation reaction is of interest for the synthesis of polyorganosiloxane oligomers [64-66]:



where R = CH_3 or C_2H_5, R′ = C_2H_5 or C_6H_5, and R″ = C_2H_5 or C_6H_5.

The method permits a specific heteromolecular condensation and homomolecular condensation can be prevented. This reaction can be included in the category of heterofunctional reactions, which were investigated in detail previously [3,4], but it has the advantage that it proceeds under milder conditions (40–80°C) at a high rate and with a high degree of conversion [66,67]. It also makes it possible to synthesise organocyclosiloxanes with known positions of the dialkyl(aryl)siloxane units in the ring [67]:



where R = CH_3 or C_2H_5, R′ = C_2H_5 or C_6H_5, R″ = C_2H_5 or C_6H_5, and R‴ = C_6H_5.

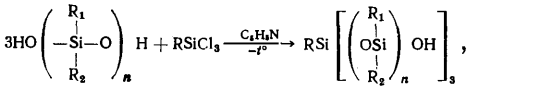
The X-ray diffraction studies, directed by Andrianov, on industrial and laboratory specimens of high-molecular-weight dialkyl(aryl)siloxane elastomers merit special consideration [68-73]. These investigations greatly amplified and extended the available data concerning the nature and physical properties of viscoelastic polydialkyl(aryl)siloxanes. The study of the effects of temperature, duration of exposure to a given temperature, deformation, the number and type of modifying groups, vulcanisation, and the amount and type of filler on the crystallisation processes of polydimethylsiloxanes (in the temperature range between −45° and −120°C) permitted a clear assessment of the influence of the above parameters on the process.

When modifying groups are introduced into the polymer, the rate and degree of crystallisation are described by relations with extrema [68,69]. The type of modifying groups does not have a significant influence on the crystallisation process. Vulcanisation [70] of polysiloxane elastomers affects the crystallisation processes like the introduction of modifying groups. The maximum rate of crystallisation is observed in the presence of an open vulcanisation network ($n \simeq 3000$). The introduction of a filler [71] accelerates the primary crystallisation process, because the filler orients on the surface the sections of the macromolecules which function as crystallisation nuclei. The rate of secondary crystallisation decreases with increase of the amount of filler and with increase of its activity. The crystallisation of deformed specimens proceeds via stages with an amorphous texture, the temperature of the onset of crystallisation being displaced towards higher values [72,73].

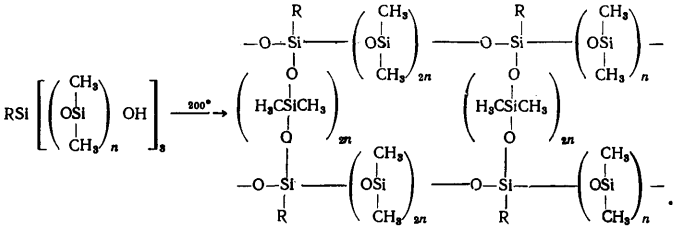
III. POLYMERS WITH CYCLONETWORK MOLECULAR STRUCTURES

The series of studies by Andrianov and coworkers described in this section was devoted to the investigation of a special class of polymeric compounds. This group of polymers is distinguished by a branched and partly cross-linked structure in which the siloxane bridges which behave as the cross-linking elements are polymeric. These compounds are obtained as a rule by polycondensation methods. Their synthesis makes it possible to regulate the distribution of the various groups or atoms in the polymer chain, which enables one to create polymers with a specified molecular structure and to regulate the properties of the polymers, whereas traditional hydrolytic polycondensation methods with subsequent catalytic polymerisation of the hydrolysis products as a rule lead to polymers with a non-order distribution of structural units.

The method of synthesising polyalkyl(aryl)siloxanes from polyfunctional oligomeric blocks is of interest for the preparation of polymers with an ordered structure [74-80]. Trifunctional alkyl(aryl)siloxane oligomers were synthesised in accordance with the scheme [81,82]

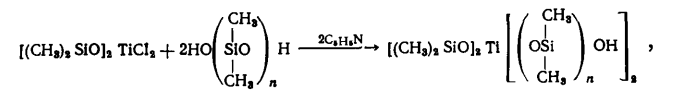


where R, R_1, and R_2 = CH_3 or C_6H_5 and n = 2, 6, 9, 14, or 32. The polycondensation of such oligomers leads to polymers with an ordered structure:

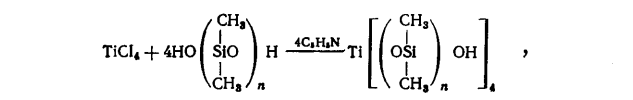


Polymers having this structure are thermoelastic and have satisfactory dielectric parameters [68]. The latter property is a consequence of the characteristic features of the method of synthesis of the polymers from oligomeric blocks. The polymers obtained by this procedure contain virtually no low-molecular-weight products and the polydispersity coefficient of the final product is low. The capacity of such polymers for crystallisation on cooling depends on the chain length between the cross-linking points. A polymer with a chain comprising 64 siloxane units crystallises in the temperature range between −67° and −72°C. When there are 18 siloxane units between the bridges, the polymer does not crystallise and passes to a vitreous state [68].

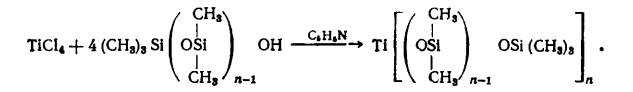
Compounds having a similar structure and containing polyfunctional metal atoms at the branching centres were obtained by heterofunctional condensation reactions. Titanodimethylsiloxane oligomers with linear and branched structures were obtained as follows [83-90]:



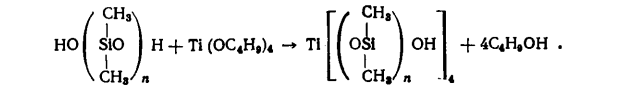
where n = 9, 22, 34, 42, and 52, and



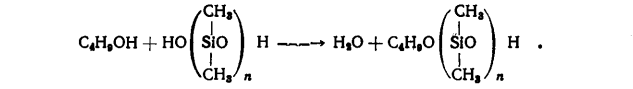
where n = 5, 13, 22, 25, 34, 42, 48, 52, 68, 80, or 104;



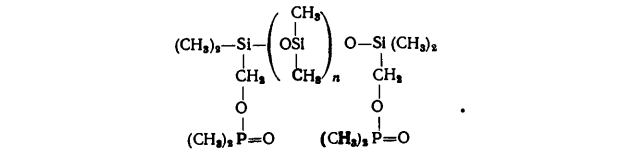
Compounds with this type of structure can also be obtained on the basis of tetrabutoxytitanium [90]:



The reaction proceeds in the above direction only when butanol is rapdily removed from the reaction sphere; otherwise the water formed in the reaction hydrolyses tetrabutoxytitanium to titanium dioxide:

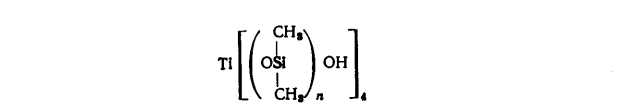


Oligomers having the above structure can react with the hydroxy-groups at the ends of the branches with formation of association complexes. As the concentration of hydroxy-groups increases (with decrease of the length from 34 dimethylsiloxane units to 13), they are gradually transformed from viscous liquids into gel-like substances. The above intermolecular interaction also leads to an increase of the packing density of the molecules. Similar features were likewise noted for polydimethylsiloxane oligomers with terminal dimethylphosphinate groups [85,86]:

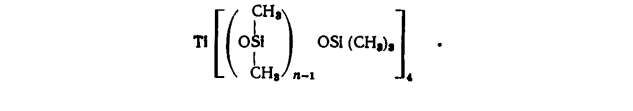


The activation energy for viscous flow, the density, and the refractive index increase with decrease of the distance between the terminal groups, which can be explained by the intensification of the interaction between the molecular chains with increase of the concentration of the polar groups per unit volume.

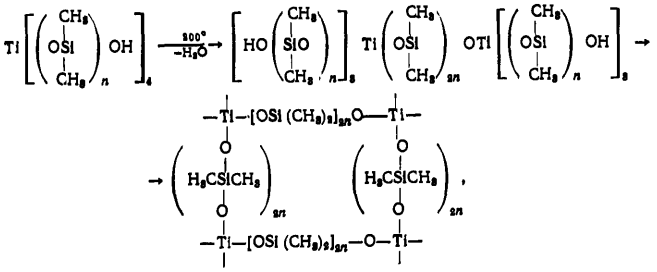
The variation of density with the length of the dimethylsiloxane chain for compounds of the type



is of a type opposite to that observed for the compounds [84]



The formation of polymers with a cyclonetwork structure [89] on condensation of branched oligomers proceeds in two stages via the formation of a soluble polymer:



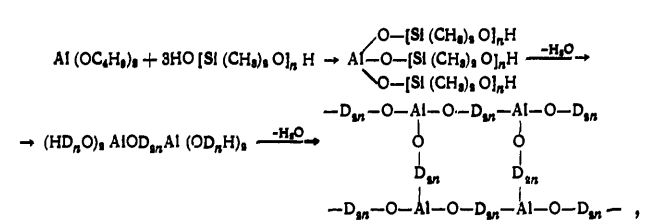
where n = 9, 18, 22, 25, 34, 42, 52, 62, 80. The structure formation reaction is first order and the structure formation rate constant decreases with increase of the average degree of polymerisation n in the initial oligomer. As the cyclonetwork structure develops in the polymer and solubility is lost, the polymer remains in the viscoelastic state up to 350°C.

X-Ray diffraction studies on these compounds showed [91] that they are amorphous at room temperature and their structure consists of packed bundles of dimethylsiloxane chains analogous to the packing of the molecular chains in polydimethylsiloxane. On cooling, the substances crystallise in the same temperature range as polydimethylsiloxane. It is interesting that, with increase of the hydroxy-group content in the compounds, the rigidity of the system rises, crystallisation is hindered, and the polarisability and dielectric losses increase [91].

A study of the thermal degradation of polytitanodimethylsiloxanes *in vacuo* showed [92] that degradation with rupture of the siloxane linkage and the formation of hexamethylcyclotrisiloxane is the rate-determining process. However, the introduction of a titanium atom into the siloxane chain appreciably reduces the rate of degradation. The rupture of the Si–O bond is accompanied by the homolytic rupture of the Si–C bond with liberation of hydrogen, methane, and ethane [93].

Compounds having a similar composition were obtained by the heterofunctional condensation of aluminium butoxide with difunctional oligomeric polyalkyl(aryl)siloxanes [94–97].

In this case the branching centre is the aluminium atom. The reaction proceeds in several stages:



where D designates the dimethylsiloxane unit $(CH_3)_2SiO$. A cross-linked polymer with a cyclonetwork structure is formed in the final stage of the process. The gel-formation rate constant depends little on the chain length of the initial oligomer, but amounts to 3.7×10^{-2}–1.4×10^{-2} h^{-1} when n for the oligomer ranges from 20 to 177 for a formally first order of the reaction with respect to the yield of the gel.

Thermal degradation of polymers of this type takes place in the temperature range 275–450°C. The main product is hexamethylcyclotrisiloxane and at 350°C methane and ethane are formed. The activation energy and the reaction order hardly depend on the distance between the nodes of the network. In this case the degradation process is a complex multistage reaction in which one can distinguish (a) thermal polycondensation in the initial stage, (b) random degradation of the polymer chain with formation of low-molecular-weight cyclic products, and (c) abstraction of organic groups from the silicon atom [92,93].

The polymers with a cyclonetwork structure examined in this section together with linear and branched polydimethylsiloxanes are convenient objects for the investigation of physicochemical properties.

A series of such studies greatly extended the existing knowledge of the nature of the siloxane chain in polymers having different structures [98–109]. An electron microscope study of polyalumino- and polytitano-dimethylsiloxanes showed that in both soluble and insoluble states these polymers have a two-stage globular supermolecular structure which is apparently of a type common to cross-linked viscoelastic polymers [98–101]. In the course of crystallisation the only structural form of polydimethylsiloxanes and polymetallodimethylsiloxanes comprises spherolytic formations. With increase of the distance between the metal atoms in the chain, the degree of crystallinity increases [102,103] together with the rate of crystallisation, which approaches the rate for high-molecular-weight polydimethylsiloxanes [100]. It is interesting that the above relation is much more pronounced for aluminium atoms at the nodes of the network than for titanium atoms.

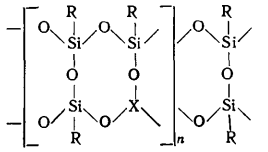
The somewhat specific character of the mechanical properties of the polymers (dependence of the modulus of elasticity, tensile strength, and deformation on n) is associated with the characteristics of the molecular and supermolecular structures [102,103]. The degree of structure formation in polyaluminodimethylsiloxanes can also be estimated by studying the relaxation properties. It was found that the increase of the equilibrium stress at the end of relaxation is faster for polymers with a low value of n. This conclusion agrees well with data obtained in a study of the kinetics of three-dimensional condensation and can be expressed by the relation $\lg \sigma_\infty = A - B \lg n$, where σ_∞ is the equilibrium stress at the end of relaxation, n the length of the siloxane chain between the nodal aluminium atoms, and A and B are constants characterising the given polymer.

The above relation makes it possible to investigate polymers in those cases where the lack of solubility precludes the investigation of the polymer structure by the usual methods [102,103].

IV. POLYMERS WITH CYCLOLINEAR LADDER MOLECULAR STRUCTURES

The possibility of the existence of polymeric molecules with a cyclolinear structure was first suggested by Andrianov together with one of the authors of the present review [104] and was subsequently confirmed by studies discussed in detail in a monograph [4]. Further investigations were directed towards finding new ways of synthesis and also to study the possibility of obtaining polymers having this structure, a high molecular weight, and different compositions of the elementary units. These compounds, which were subsequently called in the literature "ladder

polymers", have chain units with a silsesquioxane structure and can be represented by the general formula



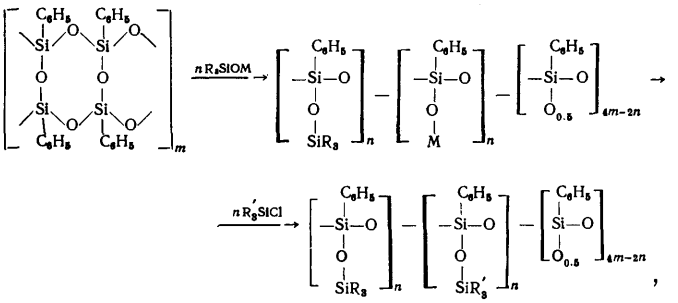
where X = Si, Al, Ti, Sn, etc.

A high-molecular-weight polyphenylsilsesquioxane, obtained initially by the high-temperature condensation of the hydrolysis product of trichlorophenylsilane [105], was subsequently obtained also by the polymerisation of a crystalline octamer [106] having the composition $(C_6H_5SiO_{4.5})_8$. In a series of tested polymerisation solvents (diphenyl ether, Dowtherm, nitrobenzene, anisole, and dimethylformamide) dimethylformamide proved to be best. In this case it is possible to obtain a polymer with a specific viscosity of 5.8. The polymer yields transparent films with a glass point above 400°C. The weight losses on heating to 500°C are 1.5–3.5% and not more than 15% at 600°C. The main polymer chain remains virtually unchanged up to 900°C. [107]

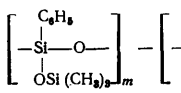
The specific structure of the molecule of the cyclolinear polyphenylsilsesquioxane in many respects determines its unusual physical properties. Thus the optical anisotropy of the molecules of this polymer exceeds by a factor of tens and hundreds the analogous parameters of the linear polymethylphenylsiloxane [108]. The number of monomer units per segment calculated from the experimental data is approximately 50, which exceeds by a factor of 10 the corresponding value for polymethylphenylsiloxane. This constitutes additional confirmation of the two-chain structure of the molecules of this ladder polymer. It is interesting that the high rigidity of the chain has little influence on the rotational mobility of the phenyl side groups [108]. It was noted that different specimens of the ladder polyphenylsiloxane have appreciably different molecular rigidities. This can be accounted for by the different proportions of structural defects in the molecules [109]. The nature of the flexibility of the ladder polymeric structure is different from that in linear polymers. It has a microdeformation mechanism (and not a rotational isomeric mechanism) involving microdistortions of the valence angles in the thermal vibrations of the atomic groups.

Appreciable differences between the structures of ladder polyphenylsiloxanes were also observed in a study of their hydrodynamic properties [110]. The values of the parameter a in Mark–Kuhn–Howink equation vary in the range 0.63–1.29.

The above investigations established that, regardless of the nature of the initial monomer, the synthesis of the polymers leads to two types of macromolecular structures. For each type of structure, there is a specific Mark–Kuhn–Howink equation. An electron microscope study on these two types of structures showed that they produce different supermolecular structures. Polymers with $a > 1$ give rise to structures of the fibrillar type and those with $a < 1$ give rise to globular structures. High values of the parameter a can be explained only by the high rigidity of the macromolecules, which causes appreciable deviations of the molecular coils from the Gaussian type even in the region of high molecular weights. The chemcal properties of the ladder polyphenylsilsesquioxane are determined by the high positive charge on the silicon atom and the negative inductive effect of the phenyl group, which increases the reactivity of the polymer in relation to nucleophilic agents. A polymer with a molecular weight of 30 000–40 000 was chosen for investigation. The reaction, carried out in accordance with the scheme

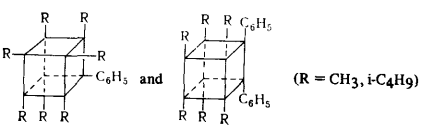


leads to oligomers with the above structure and a molecular weight of 1000–4000. [111,112] The ratio of units of different structure is statistical. Rearrangements of the siloxane skeletons with formation of six-membered structural fragments take place in the course of the above reaction together with the rupture of the silsesquioxane chain. The interaction of polyphenylsilsesquioxane with hexamethyldisiloxane at 250–260°C [113] leads to the formation of oligomers of the type



The analogous reaction with octamethylcyclotetrasiloxane [114] at 250°C leads to products with a viscosity smaller by a factor of 20 than that of the initial polyphenylsilsesquioxane.

A series of studies have been made on the synthetic possibilities and properties of ladder polymers containing, together with phenyl groups at the silicon atom, also groups with a different composition [115–129]. The synthesis and investigation of three-dimensional cyclic compounds of the type



(where each vertex contains a silicon atom and each edge represents a siloxane linkage) established that the introduction of electron-accepting phenyl substituents into the cage compounds is a necessary condition for their polymerisation, but is insufficient for their rearrangement to cyclolinear ladder polymers.

Cohydrolysis of a mixture of various alkyl(aryl)trichlorosilanes to compounds with a polycyclic structure and subsequent anionic polymerisation established a number of characteristics of the formation of the ladder structure [117,118]. An increase of the content of aliphatic substituents in the polycyclic systems decreases the rate of polymerisation. This effect is more pronounced the greater the length of the hydrocarbon chain of the alkyl substituents.

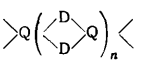
Compounds with alkyl substituents containing not more than three carbon atoms (regardless of the structure of the organic group) give rise to three-dimensional structures on polymerisation. The most favourable conditions for the formation of a ladder polymeric molecule arise when a double bond is introduced into the hydrocarbon chain of the substituent in the α-position relative to the silicon

atom. A similar effect is achieved when substituents are introduced into the phenyl group in the β-position relative to the silicon atom. The study of the hydrodynamic and dynamo-optical properties of the above polymers and of poly-3-methylbut-1-enylsilasesquioxane [123,124,129] made it possible to estimate the skeletal rigidity of the macromolecules. The thermomechanical and mechanical properties of these polymers [120,127] depend on the nature of the surrounding groups, the film-forming capacity being retained when the composition of the chain unit is altered. The thermal stability of ladder polymers greatly exceeds that of linear polyorganosiloxanes [121,126,127].

V. POLYMERS WITH SPIROCYCLIC AND SPIROLADDER MOLECULAR STRUCTURES

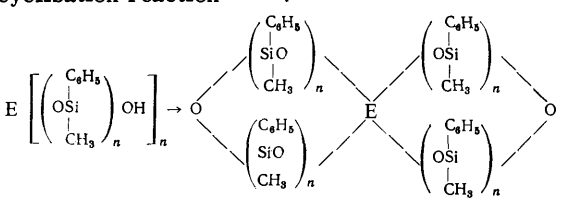
This class of polymers, which have an extremely unusual structure of the main molecular chains, opens a new chapter in the chemistry of organosilicon polymers, which has been developed very vigorously in recent years by Andrianov [128].

Polymers of this group contain cyclic fragments linked to the atom of an element forming part of two rings which constitute the molecular chain. The structure of a spirocyclic polymer can be represented schematically as follows:



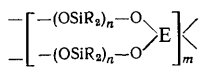
where D are bifunctional fragments and Q is the spirocyclic centre (a silicon or a polyvalent metal atom).

The possibility and ways of synthesising such polymers were predicted by earlier studies [137]. Thus it was noted that, when cross-like oligomers of type $E[(OSiR_2)nOH]_4$ are condensed, polymers with a molecular network structure are formed only when the distance between the central atom E and the functional group is large. The condensation of oligomers with small values of n leads to soluble polymers, which can be accounted for by an intramolecular cyclisation reaction [136,137]:



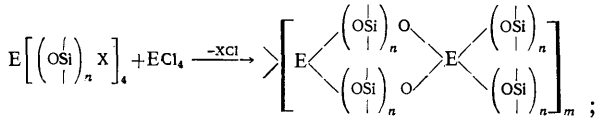
The compound with $n = 1$ is crystalline (E = Si), while those with $n = 3$ (E = Si or Ti) are amorphous under the usual conditions.

This reaction also involves the formation of a soluble polymer without hydroxy-groups. Thus the reaction proceeds simultaneously with intermolecular condensation and formation of polymers of the type

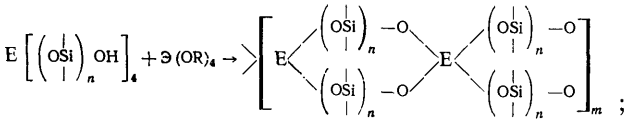


The following reactions have been used to synthesise spirocyclic polymers [128]:

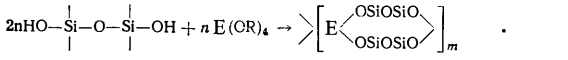
(1) exchange reactions:



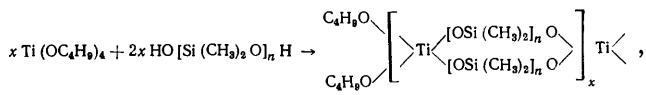
(2) polycondensation of tetrafunctional compounds:



(3) condensation of bifunctional compounds with tetrafunctional compounds:

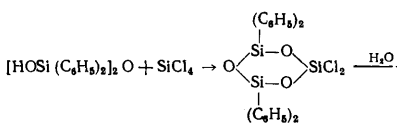


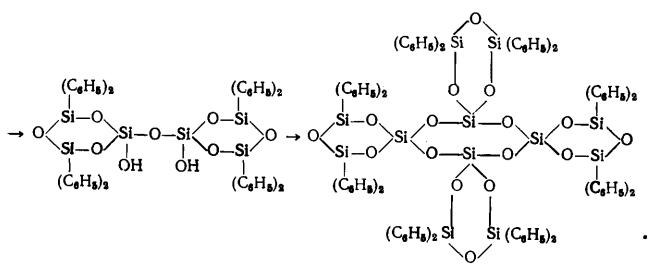
For example, polyspirotitanodimethylsiloxanes were obtained by the reaction [138]



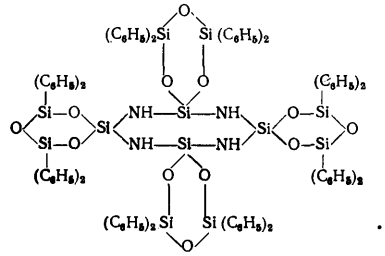
where $n = 2$, 3, or 4 and the molecular weight reaches 2000–3500. The low degree of polycondensation can be accounted for by the steric hindrance suffered by the reactant molecule on approaching the functional groups of the molecule of the polymer being formed. The spiro-structure of the resulting polymer is stable up to 300°C, [139] the spirocyclic fragments in the polymer molecules undergoing a rearrangement only at 400°C. Hydrodynamic and optical studies on these polymers [129] demonstrated the presence of a high degree of intramolecular order and a high equilibrium rigidity of the macromolecules.

One of the ways of obtaining polymers with a spirocyclic structure is catalytic polymerisation of organospirosiloxanes. The initial spiro-compounds were obtained by a multistage synthesis [130–133]:

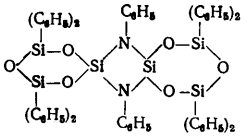




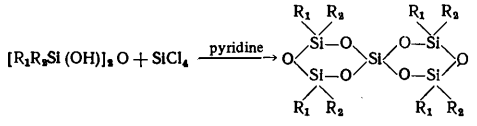
The last stage proceeds with difficulty and only at 280–300°C (owing to the screening effect of the diphenylcyclotrisiloxane fragments). The replacement of the second, hydrolytic stage in the above scheme by ammonolysis with ammonia makes it possible to obtain a silazane–siloxane spiro-compound:



On the other hand, when the ammonolysis is carried out with aniline, it is possible to obtain ultimately by the above scheme a spiro-compound with a four-membered silazane ring:

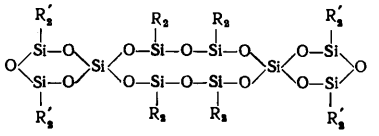


The above syntheses were achieved in the absence of a hydrogen chloride acceptor in the first stage. On the other hand, in the presence of pyridine, the spiro-compound is obtained in one stage:

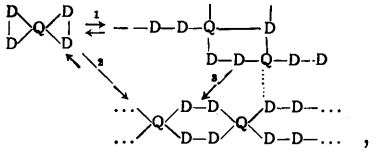


where R_1 and R_2 = CH_3 or C_6H_5.

In the course of high-temperature distillation these compounds partly rearrange to higher spirocyclic products:



It is interesting that the formation of cross-linked products is not observed. When organospirobicyclosiloxanes are subjected to anionic polymerisation in bulk [134,135], the growing polymer chain is involved in two competing reactions (intermolecular and intramolecular interactions). This can be represented by the scheme

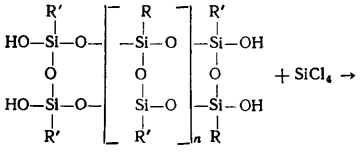


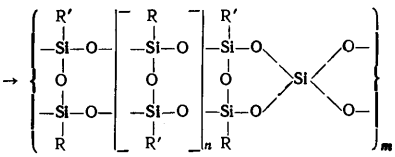
where D are bifunctional fragments and Q are tetrafunctional fragments.

The process proceeds both with formation of soluble (pathway 2) and cross-linked products (pathway 1). The content of the gel fraction falls as the surrounding methyl groups are replaced by phenyl groups. When the molecule of the initial compound contains exclusively phenyl groups, the gel is not formed.

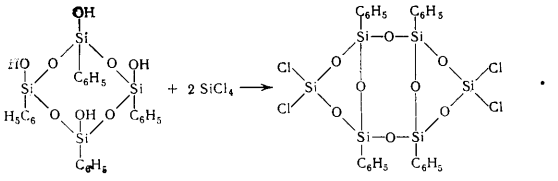
The polymerisation of the above compounds in dilute solutions [134] as a rule leads to the exhaustion of the initial cyclic fragments.

Compounds having polymer chains containing simultaneously fragments with spiro- and ladder structures constitute a special group of polymers. In their synthesis by heterofunctional condensation the most favourable conditions for the formation of the expected structure occur when the initial stage of the reaction proceeds at a low temperature in not too dilute solutions [140,141]:



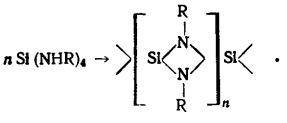


where R = C_6H_5, R′ = i-C_4H_9 or C_6H_5, and n = 0–2. The length of the cyclotetrasiloxane fragment (the value of n) affects the possibility of obtaining spiro-groups. For n = 2 and R = R′ = C_6H_5, it proved possible to obtain polymers with a characteristic viscosity of 0.12–0.22 dm g^{-1}, while for n = 0 the expected structures could not be produced. These results were explained by stepwise condensation:



The polycyclic compound formed has the *cis*-structure like the initial tetrol $[C_6H_5Si(OH)O]_4$. When the resulting polycyclic compound reacts with an equimolar amount of the tetrol, spiro-groups are not formed owing to the *cis*-conformation of the reactants.

The study of the hydrodynamic and optical properties of polyisobutylphenylsiloxane with a spiroladder structure [142] showed that the molecules have the properties of fairly flexible non-fluid coils, resembling Gaussian coils from the hydrodynamic standpoint. Such flexibility can be accounted for by structural defects. On the other hand, the behaviour of polymethylphenylspirosiloxane molecules (with 8 and 16 atoms in the ring) in solution differs from the usual behaviour of semirigid regular chains with both small and large segments, which can be explained from the standpoint of non-linear structures of the network type [141]. Spirocyclic polymers with a silazane structure [128] were synthesised by the reaction

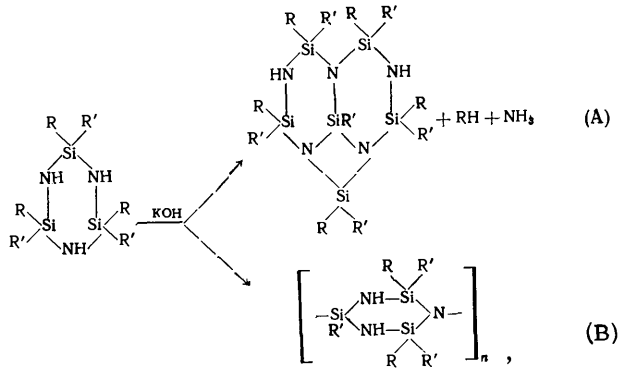


VI. POLYORGANOSILAZANES

Great hopes were associated with studies on polyorganosilazanes because there are many unsolved problems related to the synthesis, structures, and properties of organosilicon polymers, which could not be solved solely in relation to compounds of the siloxane series.

The reaction of organocyclosilaxanes with nucleophilic agents is the most promising from the standpoint of polymer chemistry. However, it differs appreciably from the analogous reaction of organocyclosiloxanes. In the first place, in contrast to organocyclosiloxanes, organocyclosilazanes exhibit a greater tendency to undergo substitution reactions than addition reactions. In this respect their properties resemble aromatic systems [142,143]. The reaction of dialkyl(aryl)cyclosilazanes with nucleophilic agents [144–154] is accompanied by the evolution of the hydrocarbon corresponding to the organic group attached to the silicon atom and the formation of cyclic polymers which soften at a high temperature. When the silicon

atom is surrounded by aliphatic groups, the reaction proceeds as follows:

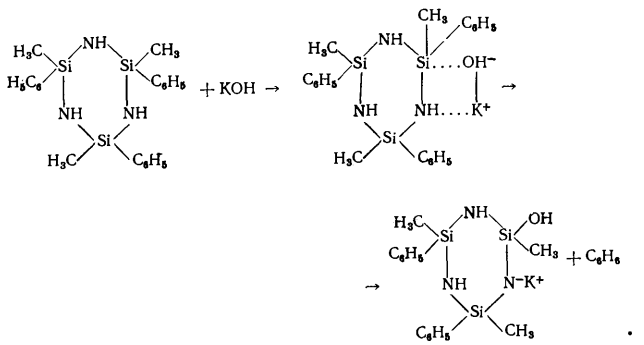


(A)

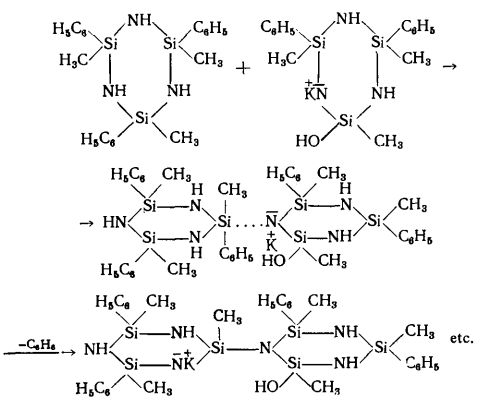
(B)

where R = CH_3 or C_2H_5 and R′ = C_2H_5, C_4H_9, or C_6H_{13}. It is interesting that compound (A) is chemically inert and remains unchanged when acted upon by catalytic amounts of alkali. The product (B) is formed via condensation without ring opening and not via compound (A).

The anionic polymerisation of methylphenylcyclosilazanes also does not proceed via ring opening, but involves the formation of a transition complex which weakens the Si–C bond and not the Si–N bond:



The subsequent reaction proceeds via the coordination of the molecules of the initial compound to the resulting anion, which contains the $\rangle N^-$ fragment:



The resulting polymers have a filamental or branched structure. An increase in the bulk of the organic group at the silicon atom stabilises the transition complex and hinders its conversion into the active state. As a result, the reaction rate falls sharply. The reaction involving trimethyltrinonylcyclotrisilazane does not begin up to 300°C. The influence of the groups surrounding the silicon atom is also associated with steric effects. Bulky groups (hexyl, octyl, and nonyl) hinder the polymerisation.

Studies on the possibility of synthesising polymers with silazoxane chains [155–159] revealed the fundamental pathways leading to the formation of polymers of this type. The synthesis of the polymers by the condensation method proved to be promising [157–159]:

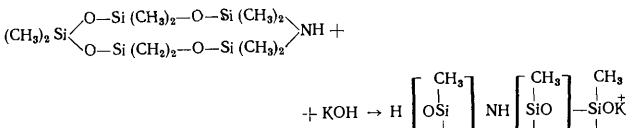
$$RN(H)[Si(CH_3)_2O]_n Si(CH_3)_2NHR \xrightarrow[-RNH_2]{t^\circ} \rightarrow R(H)N\{[Si(CH_3)_2O]_n Si(CH_3)_2NR\}_m H,$$

where R = H or C_2H_5 and $n = 4-10$, 11, or 40.

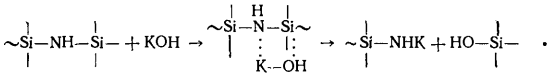
The polymers consist of swelling insoluble substances with a distinct region of a viscoelastic state. A study of the thermo-oxidative degradation of these polymers showed [160] that the introduction of a nitrogen atom into the siloxane chain stabilises it to some extent.

The anionic polymerisation of cyclosilazoxanes containing hydrogen at the nitrogen atom was unsuccessful.

The ring is opened initially at the siloxane linkages:

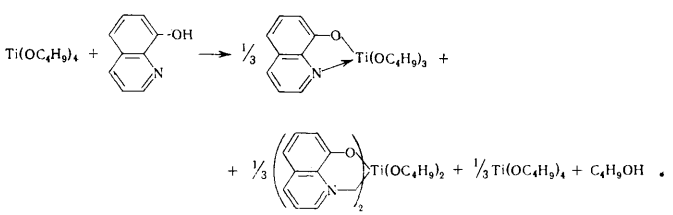


In the second reaction stage the polymeric chains are ruptured at the silazane linkages:

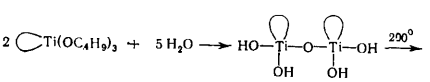


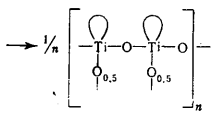
VII. POLYORGANOSILOXANE DERIVATIVES OF THE ELEMENTS

Polymers of this class were synthesised for the first time and investigated in detail by Andrianov's School. The main bulk of studies in this field have been described in a monograph [4]. Some of the investigations formally concerned with this field were examined in the preceding sections of the present review. This section deals with certain investigations published after the publication of Andrianov's monograph [4]. Numerous studies were devoted to polytitano-organosiloxanes. The replacement of one or two butoxy-groups in tetrabutoxytitanium by 8-hydroxyquinolinato-groups makes it possible to reduce the number of groups with which the titanium atom can interact to three and two respectively [161]:

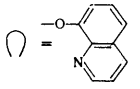


Hydrolysis of the tributoxy-compound with subsequent thermal condensation leads to polymers having a metalloxane structure [162]:

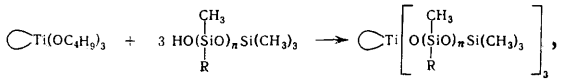




where



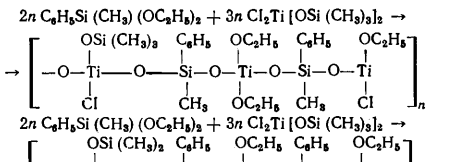
The reaction of the above trifunctional compound with hydroxylated polysiloxane oligomers leads to the formation of branched oligomers [163,164]:



where n = 15, 60, 98, 170, or 350 and R = CH_3 or C_6H_5.

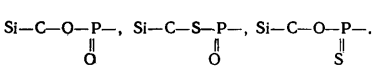
The resulting oligomers proved to be convenient model compounds for the study of the dependence of physicochemical properties on the siloxane chain length. It is interesting that the polydispersity coefficient of the oligomers does not differ significantly from that of the initial hydroxylated polyorganosiloxanes. The presence of 8-hydroxyquinolinatotitanoxane groups intensifies the intermolecular interaction and the packing density of the molecules, which affect the density, activation energy for viscous flow, and the free volume of the resulting oligomer [165]. An increase in the length of the siloxane chain in the branches has the opposite effect on the above parameters. The competing effects of various structural elements are observed particularly clearly in studies on the dynamic viscosity of oligomers. It has been established [164] that the introduction of 8-hydroxyquinolinatotitanoxane groups into polydimethylsiloxanes increases their thermal stability and the oligomers mentioned above are effective inhibitors of the thermo-oxidative degradation of liquid polydimethylsiloxanes.

Polymers with an unusual structure of the main chain, containing alternating titanium and silicon atoms, were obtained by heterofunctional condensation [166]:

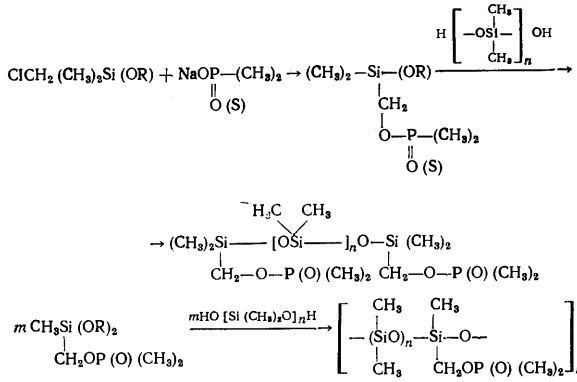


The resulting polymer is a viscoelastic product, which can be readily drawn into threads. Owing to the presence of hydrolysable groups the polymer is not resistant to moisture.

A number of studies have been made on the synthesis and properties of polyorganosiloxane polymers containing phosphorus atoms in the side chains [167-171]. In contrast to the majority of earlier studies on the nature of the Si–O–P linkage, the above series of investigations was devoted to compounds containing the groups

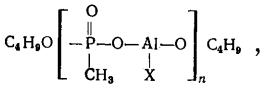


Such groups are much more resistant to hydrolysis than the Si–O–P group. Compounds of the siloxane series containing phosphinate groups or their thio-analogues in the methyl substituent at the silicon atom are synthesised by the reaction

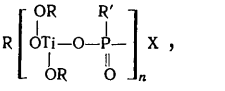


where n = 9, 13, 45, 75, or 130. By altering the proportions of the dimethylphosphinate and dimethylsiloxane groups, it is possible to vary the properties of the polymers within wide limits.

In this section of the review it is appropriate to mention studies dealing with methods for the synthesis of polymers with inorganic main molecular chains, without silicon atoms. These are primarily polyaluminomethylphosphonates [172-175]

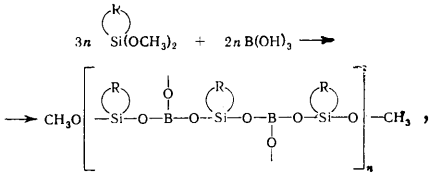


where X = Cl or C_4H_9, poly(dialkylphosphinyl)titanoxanes $\{[(CH_3)_2P(O)O_2TiO]\}_x$, [176,177] and polytitano-organophosphonates [178-180]

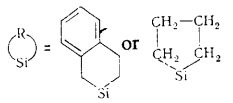


where R = C_4H_9, R′ = CH_3 or $CH_2{=}C(C_6H_5)$, and X = Cl, OH, or OC_2H_5. A detailed study of the properties of polytitano-organophosphinates established that their degradation at temperatures up to 400°C involves only the abstraction of the organic groups with retention of the Ti–O–P linkage [197,202]. It was established that these compounds can be used as thermostabilisers to improve the heat resistance of polyorganosiloxane varnishes and enamels [206]. The introduction of an organophosphinoxytitanoxane group into polyorganosiloxanes increases the resistance of the latter to thermo-oxidative degradation [202,203]. These results constituted the basis for the formation of siloxane resins with enhanced thermal stability [204,205].

Polyorganosiloxanes containing boron have been described [181-188]. Polymers with very variable compositions have been studied. Polyborosiloxanes containing silicon atoms in the main chain and at the same time silicon atoms behaving as the heteroelement in the heterocycle were obtained by the reaction

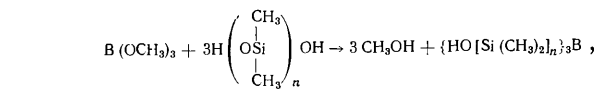


where

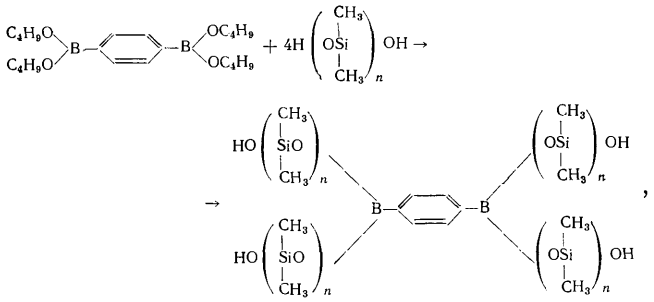


Polymers with this composition have a high resistance to thermo-oxidative degradation [186-188].

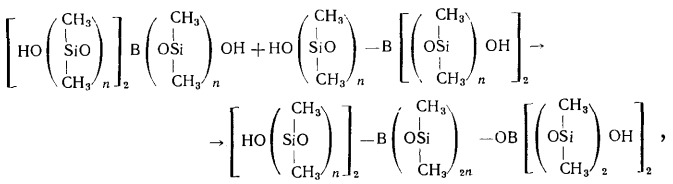
Branched polyborodimethylsiloxanes are synthesised by heterofunctional condensation [181-183]:



where n = 9, 13, 25, 45, 74, 135, or 220,

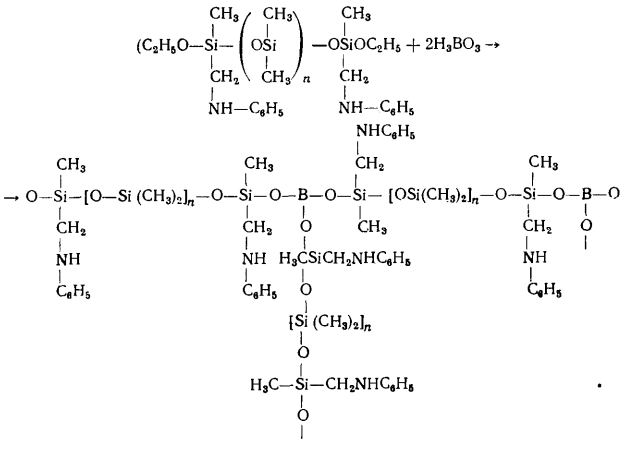


where n = 30, 46, 76, 95, or 235, and by homofunctional condensation [184,185]:



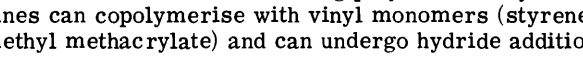
where n = 13, 25, 46, 74, or 200.

In the last of the polymers quoted the boron content is insignificant, and yet leads to an appreciable improvement of thermal stability compared with polydimethylsiloxanes [189]. The resistance of the SiOB linkage to hydrolysis was increased by the introduction of phenylaminomethyl groups among the organic substituents surrounding the silicon atom [183]:



The reason for the increased resistance to hydrolysis is in this case the formation of a coordinate bond between the nitrogen atom of the phenylaminomethyl group and the boron atom, which hinders the formation of a transition complex with water in the hydrolysis of these compounds.

A comparatively new development in the field of polymeric organosiloxane derivatives of the elements is the synthesis of polymetallo-organosiloxanes with reactive groups at the silicon atom, in particular vinyl groups [190-193]:



where M = Al or Ti. The resulting polymetallovinylsiloxanes can copolymerise with vinyl monomers (styrene and methyl methacrylate) and can undergo hydride addition reactions with compounds containing the SiH group. Both methods make it possible to vary widely the properties of the polymers both as a result of a change in the nature and amount of the metal introduced into the polymer and as a result of the selection of the appropriate vinyl monomer. The products of the addition of polytitanovinylsiloxanes to polyorganoaluminosiloxanes proved to be very effective components of heat-resistant adhesive compositions [193].

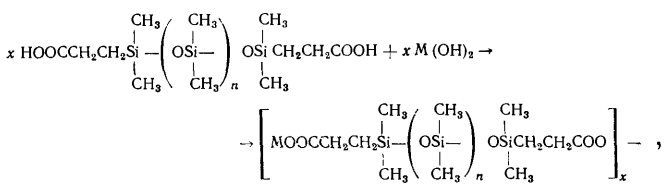
Polymeric organosiloxane derivatives of the elements constitutes a class of polymers differing from the majority of organic polymers, primarily by their high heat resistance. It is therefore quite natural that numerous studies have been devoted to the thermal and thermo-oxidative degradation of polymers of this class [189,194,201,207,208,209].

The above series of studies established the relation between the structure of the polymer unit, the nature of the heteroatom, the composition of the organic group at the silicon atom, and many other structural characteristics on the one hand and the thermal stability of the polymer on the other.

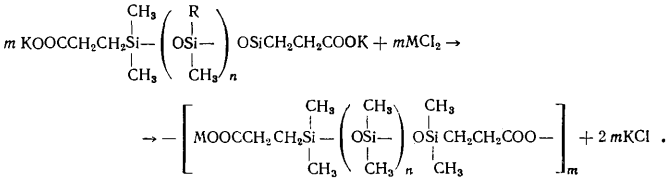
In conclusion of this section, we shall mention a number of studies on the synthesis and properties of polydimethylcarboxyatometalloxyloxanes containing metal atoms in the main chain linked to a silicon atom via a carboxylate group [212-222].

An attempt to introduce bivalent metal atoms into the siloxane chain was described in earlier investigations [210,211] and was found to involve many difficulties. A series of studies by Andrianov and coworkers [212,222] constitutes the most successful attempt at the introduction of bivalent metals into the siloxane chain, the carboxylate groups surrounding the metal atoms determining in many respects the unusual properties of these polymers.

The polymers were synthesised in two ways: (a) from the metal hydroxides:

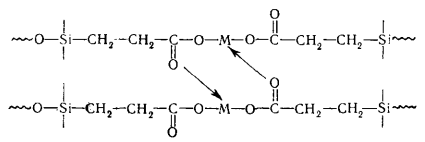


where M = Ca, Zn, Cd, Pb, or Co, and (b) from the metal chlorides:



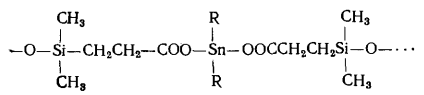
With increase of the distance between the metal atoms in the polymer chain, the viscosity of the polymer rises. Polymers with n = 20 are already rubber-like. Those with n = 50–70 are insoluble in the usual organic solvents

owing to the marked influence of interchain coordinate bonds of the type



The polymers become soluble when 2–3% of pyridine, which disturbs the above interactions, is introduced into the system. The presence of such linkages is also indicated by the high yield temperatures of the polymers and the high viscosities of the low-molecular-weight oligomer products of this type.

An additional confirmation of the presence of coordinate bonds in polymers of this kind has been provided by the study of a polymer based on quadrivalent tin, where such interactions are ruled out:



The properties of this polymer differ appreciably from those described above. Assuming the possibility of the formation of coordinate bonds between polymetallodimethylsiloxane macromolecules and their influence on the thermomechanical properties of the polymers, the metals investigated can be arranged in the following sequence in terms of decreasing intermolecular interaction forces due to these linkages [217,218]: Co > Zn > Pb,Ca > Cd.

This series agrees well with the order of decreasing coordination capacities of the metals. Studies on solutions of these polymers showed that, when the metal content is small (one atom for 30–100 silicon atoms), the conformation of the polymer molecule does not differ from that of the dimethylsiloxane polymers in solution [216]. It has also been established that the nature of the metal atom does not affect the rate of crystallisation of the polymers [218], but has an appreciable influence on the thermal degradation [222]. The thermal stability of the polymer increases with increasing basicity of the metal. These results together with those obtained by the chromatographic analysis of the thermal degradation products make it possible to elucidate the mechanism of the thermal decomposition of polymers of this type.

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Problems of the Chemistry of Thermostable Organic Polymers

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The effect of π-electron delocalisation, due to polyconjugation in macromolecular structures, on the thermal and thermo-oxidative stability of polymers is surveyed, and data are given indicating that thermal oxidation is activated by the centres produced by the rupture of strained chemical bonds during thermolysis. Certain general problems and advantages in the synthesis of polyconjugated thermostable oligomers and high polymers are discussed. A list of 76 references is included.

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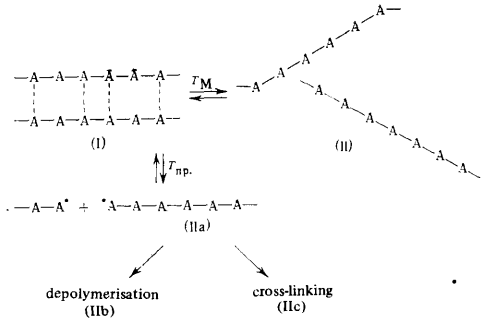
I. INTRODUCTION

The action of heat on a polymeric material may cause processes of two kinds, resulting in reversible and irreversible changes in its physicochemical properties. The first type involves phase transitions or variation in molecular mobility in amorphous regions of polymers. Such changes are taken to characterise the deformative thermal stability or thermophysical stability of polymers and polymeric materials. Irreversible change in the physicomechanical properties of polymers, in contrast, are mostly due to chemical changes in the polymer caused by the temperature and the environment. Such changes are related to the chemical thermal stability or thermochemical stability. In the absence of a reactive environment, e.g. oxygen, thermochemical degradation may be more or less reversible, although the attainment of complete reversibility is in practice difficult owing to the finite probability of anomalous recombination and cross-linking. The variation in the thermophysical stability of polymeric materials during processing and service is due in most cases to degradation and cross-linking: i.e. it is connected with their chemical thermal stability. Therefore the thermochemical stability may well be the main property from which the temperature range for practical application of the polymer can be assessed.

There are thus two states that are most dangerous in use—melting (or softening) and degradation of the polymer (beginning at a limiting temperature T_{lim})—a situation which is shown clearly by the scheme



The thermal conditions for the transition from (I) to (II) or to (IIa) are governed by the decrease in free energy $\Delta G = \Delta H - T\Delta S$, and are characterised at equilibrium by the phase transition or chemical conversion temperature $T_{tr} = \Delta H/\Delta S$. The temperature T_{tr} is obviously higher the smaller are H_{tr} and ΔS. Such conditions can be realised in polymer systems whose macrochains contain no weak chemical bonds and are characterised by strong intermolecular interaction (H_I small), as well as by a slightly larger S_{II} than S_I. This is possible in rigid systems, when the decrease in chain length on degradation produces a sharp drop in flexibility, and also during cross-linking processes.

Although the above considerations relate to thermal transformations in polymers, they have some significance for thermal oxidation processes initiated by the rupture of chemical bonds. The irreversible character of thermal oxidation and cross-linking complicate the thermodynamic treatment of the relation between the structure and the thermochemical stability of polymers, bringing a kinetic examination of the process to the forefront.

Since the thermochemical stability of polymers at high temperatures (at or above 300°C) depends primarily on the strength of the chemical and intermolecular bonds and on the molecular mobility of the structural units, we must consider the effect of electron delocalisation along the chains of the macromolecules on the thermal stability of polymeric materials. Further justification for such an approach to the problem of thermal stability is that the character of the electron delocalisation (conjugation) along large segments of polymer chains should influence not only the strength of the bonds linking them but also the molecular mobility and intermolecular interaction.

The Reviewer has repeatedly pointed out that enhancing the thermal stability (chemical and physical) of organic polymers requires the "designing" of macromolecules having a developed system of conjugation by π-electron delocalisation[1-3]. Electron delocalisation can be shown to determine the thermal stability not only of so called organic polymers but also of polymers with inorganic chains. Indeed, the data in Table 1, gathered from several sources[4,5], show that in all cases the strength of a bond is improved by its polarisation and many-centred character. From this it may be concluded that macromolecules of highly thermostable polymers can be constructed in three main ways.

1. Formation of a polyconjugated system of multiple bonds and aromatic and/or heterocyclic rings. The polymer chain then contains extended segments in which a

particular type of π-conjugation is established. Such systems possess considerable rigidity, and form stable supermolecular structures[6].

2. The building up of macromolecules by means of "quasi-cumulene"[7] dative bonds formed by the delocalisation of p-electrons of one heteroatom into d- or p-electron vacancies of another element attached to it, e.g.

Such compounds include polysiloxanes and other organometallic[8,9] and inorganic[10,11] polymers. With substances of this type (in any case those with p,d-conjugation) chain flexibility does not create conditions preventing delocalisation, since flexibility is realised not so much by rotation about valency bonds as by the deformation of bond angles[7]. Thus high elasticity can be combined here with thermochemical stability of the polymeric material.

Table 1. Effect of delocalisation of π- and p-electrons on bond energy.

Bond	Conjugation	Energy, kcal mole^{-1}	Bond	Conjugation	Energy, kcal mole^{-1}
$C_{aliph}-C_{aliph}$	—	83.0	$C_{aliph}-Si$	—	78.0
$C_{arom}-C_{arom}$	$\pi-\pi$	98.0 (105)	$Si-\ddot{O}$	$p-d_v$	106.0
$C_{aliph}-\ddot{N}H$	—	82.0	$B-N$	$p-p_v$	115.0
$C_{arom}-\ddot{N}H$	$p-\pi$	110.0	$B-\ddot{O}$	$p-p_v$	113.0
$C_{aliph}-\ddot{O}$	—	93.0			
$C_{arom}-\ddot{O}$	$p-\pi$	107.0			

Arrows: .....delocalisation of π-electrons;
----delocalisation with displacement of p-electron density;
d_v, p_v electron vacancies.

3. Formation of block-copolymer structures including fragments of π-electron conjugation[1] and organometallic or inorganic fragments with p,d-delocalisation of valency electrons. Such structures may be expected to exhibit an interesting combination of the physicomechanical properties characteristic of polyconjugated polymer systems and compounds with dative bonds[2].

In this Review we shall examine certain problems associated with the thermal stability of organic polymers containing more or less extended fragments of π-conjugation.

II. PECULIARITIES OF THE STRUCTURE AND THE THERMOCHEMICAL STABILITY OF POLYCONJUGATED SYSTEMS

It has now been shown that the high thermochemical stability of polyconjugated polymer systems is due to processes which, in the absence of oxygen, tend to extend the polyconjugated chain. The ultimate results of such changes is the formation of graphite, amorphous carbon, or products of similar electronic structure. Special allowance must be made for this fact in the study of degradative changes in polyheteroarylenes.

The conversion of "saturated"† into polyconjugated polymers and then into graphite or amorphous carbon is accompanied by a decrease in the free energy of the system. Thus calculations show[12] that, in the thermal degradation of polyethylene and several other high polymers, graphitisation is considerably more advantageous thermodynamically than are other chemical changes. This leads to the following consequences.

1. The use of polyconjugated systems to obtain thermostable materials becomes increasingly advisable the closer such polymers approach graphite in structure and thermodynamic characteristics.

2. The widely held view that the primary structure of a polymer gives adequate criteria for judging its thermal stability cannot be regarded as correct. In fact, the energetic advantage of conversion to more extensive conjugation indicates that assessment of the thermochemical stability of a polymer should be based not so much on the specified (initial) structure of a polymer as on allowing for the chemical changes and the nature of the final products formed by the action of heat and of the environment.

For example, such polymers as cellulose, poly(vinyl alcohol), poly(vinyl acetate), polyacrylonitrile, etc. are able to form highly thermostable films and fibres as a result of degradative processes yielding polyconjugated systems, and at 2000°C forming graphite structures[3,13]. This applies also to the almost colourless polytetraphenylphenylene[14], in which the arrangement of phenylene units is non-coplanar owing to the large number of substituents. When a film of this polymer is heated, it splits off benzene, and becomes coloured, less soluble, and paramagnetic. It is not surprising, therefore, that the weight losses rapidly approach a limit on heating (400–500°C) and that the material withstands prolonged heating, especially in the absence of oxygen.

3. Since growth of the polyconjugated chain during the thermolysis of polyconjugated systems entails considerable contractions and is accompanied by degradative processes, it is reasonable to pay special attention to the synthesis of polyconjugated polymers of ladder and block–ladder structure[15,16], as well as polymer chains with regularly alternating branches, including polyconjugated fragments. The increasing interest taken in the synthesis and investigation of such structures thus becomes understandable[17].

Polyconjugated systems are characterised by the formation of stable association complexes by intermolecular donor–acceptor interaction. Such aggregates probably constitute a microphase, impair the solubility of the polyconjugated system, and raise the softening or flow point above those of saturated analogues[6].

It has been shown experimentally that polyconjugated polymers belong structurally to microheterogeneous systems, since association complexes (d = 10–50 nm) pack into larger spherical supermolecular structures (d = 1–5 μm) (Fig. 1).[6] Although the question of special intermolecular forces in polyconjugated polymers and their decisive importance in the physics and chemistry of the systems was considered as long ago as 1958,[2] due attention was not paid to it by research workers until recently, when the problem was again raised in connection with the study of the formation of polyconjugated chains[7] and the structure of organic semiconductors[18–20].

† "Saturated" polymers are those not containing π-bonds conjugated through large fragments or throughout the macromolecule.

In order to elucidate this matter a calorimetric determination was made of the conjugation energy, and the contribution to it of intermolecular π-electron interaction in individual and polymeric hydrocarbons—oligoarylvinylenes and polyarylenes—was calculated[6]. The difference between the total conjugation energy and that in the benzene rings was adopted as the criterion for assessing the intermolecular exchange interaction of π-electrons of polyconjugated chains; it was termed the "structure stabilisation energy" ΔH_π.

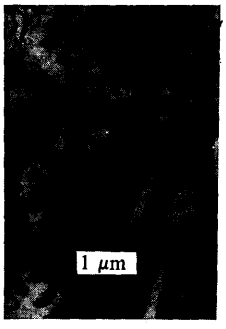


Figure 1. Electron micrograph of unshadowed platinum–carbon replica with amorphous benzene–naphthalene copolymer.

An additional contribution of 6.0–12.0 kcal mole^{-1}, appreciably exceeding known conjugation energies (2–4 kcal mole^{-1}) for buta-1,3-diene and its vinylogues, was found for individual polyene hydrocarbons containing terminal phenyl groups. It would have been wrong to attribute this difference to intramolecular delocalisation. It is more reasonable to suppose that the observed values are due mainly to intermolecular exchange interaction. On passing to polymers having a conjugated system the values of ΔH_π may exceed those found for the corresponding model systems, and may reach hundreds of kilocalories calculated for the average macromolecule. The above properties of polyconjugated systems indicate considerable intermolecular interaction and a tendency for their macromolecules to associate. The presence of strong intermolecular interactions in polyconjugated systems is largely responsible for their thermal stability, rigidity, and several other specific properties.

Existing data indicate the high radical reactivity of polyconjugated systems and its activation by paramagnetic centres present in them ("local activation effect")[6,21]. This is why self-inhibition is observed in the thermal (and at lower temperatures also in the thermo-oxidative) degradation of polyconjugated systems or "saturated" polymers capable of conversion into the former when heated[22,23]. Thus the polyconjugated polyphenylacetylene undergoes thermo-oxidative degradation considerably more slowly and to a considerably less extent than does its hydrogenated analogue, polystyrene (Fig. 2)[22,23]. With rise in temperature self-inhibition of the thermal degradation of polyconjugated systems is exhibited as far as extensive carbonisation of the polymer. The rate of the process is diminished by three-dimensional cross-linking of the polyconjugated system. The opposite results are observed with thermo-oxidative degradation: insoluble and infusible network polymers are less thermostable than their fusible and soluble analogues (Fig. 3).

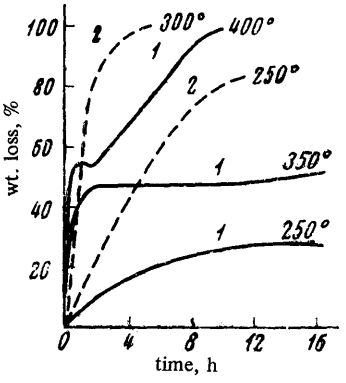


Figure 2. Thermo-oxidative degradation of: 1) polyphenylacetylene ($\overline{M}_n$ = 5000); 2) polystyrene (9000).

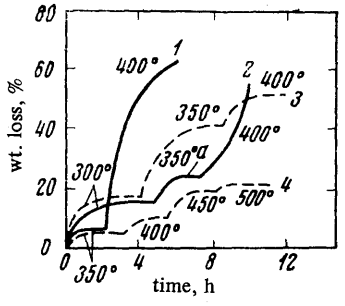


Figure 3. Weight-loss curves for: 1) three-dimensionally cross-linked insoluble block copolymer of poly-5-ethynyl-2-methylpyridine ($\overline{M}_n$ = 1700) with *p*-diethynylbenzene in air; 2) poly-5-ethynyl-2-methylpyridine (soluble fraction) in air (a = point corresponding to conversion into insoluble, infusible polymer); 3) as (2) in argon; 4) block copolymer in argon.

The probable explanation of such specific behaviour is that degradation of a polyconjugated system starts with the cleavage of weak bonds primarily in segments of disrupted conjugation. The resulting radicals can react to form a thermodynamically more stable polyconjugated structure. This process entails increased contractions and internal stresses which, at temperatures close to the carbonisation point, are able in turn to cause the local rupture of bonds. The macroradicals formed during degradation become stuck in the rigid polymer, with a greater loss of mobility the more rigid the polymer framework. The presence of radical centres having a relatively low ionisation potential catalyses the thermal oxidation. Oxygen may then be activated by the formation of charge-transfer complexes.

A different picture is observed in the thermal degradation of polyconjugated systems in the absence of oxygen, when the retained radicals probably act as traps binding active centres of the breakdown products responsible for the development of degradative processes. Convincing evidence of the creation of active centres during thermolysis is provided by our observation of reactivity in three-dimensionally cross-linked polymers (phenol–formaldehyde resites, polymers and copolymers of *p*-diethynylbenzene) thermolysed at 450–500°C. Such polymers exhibit semiconductor properties and are typical polyconjugated systems; they contain fused aromatic structures with paramagnetic centres at concentrations of $10^{19}-10^{20}$ spins g^{-1} and a narrow electron spin resonance signal (a singlet) of line width 3–4 Gauss [3,18]. Thermolysis products freshly prepared in a vacuum of $10^{-3}-10^{-5}$ mmHg possessed several specific properties: (i) their thermal oxidation passed at 300°C into combustion [24]; (ii) they were effective catalysts for the radical polymerisation of acrylates and several other electron-accepting monomers (Fig. 4) [25]; and (iii) keeping the thermolysates in oxygen, argon, or a vacuum, or the presence in the polymers of plasticisers capable of inactivating radicals (e.g. diphenylenemethanediols or phenolic alcohols in the case of phenol–formaldehyde oligomers), produces a decrease in the number of paramagnetic centres and sharp drops in the rate of oxidation of the thermolysates and in their catalytic activity towards radical polymerisation (Figs. 5 and 6).

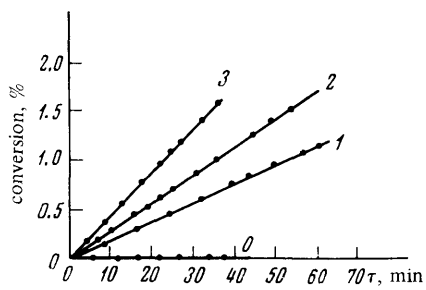


Figure 4. Variation of rate of polymerisation of methyl methacrylate catalysed by 2% of a dephenolated thermolysed phenol–formaldehyde resite with content of paramagnetic centres in the latter (spins g^{-1}): 0) no catalyst; 1) 2×10^{18}; 2) 1.7×10^{21}; 3) 5×10^{21}.

Similar regularities have been observed in the thermal and thermo-oxidative degradation of heterochain polyconjugated systems. An example is provided by results [3,26] obtained for polydiphenylamine, whose rate of degradation above 400°C is very low both in argon and in oxygen. Only on the initial portions of the rate curves are significant weight losses observed, as a consequence of the volatility of fractions of lower molecular weight and fragments of linear polymer molecules formed on degradation. The initial losses therefore increased as the molecular weight of the polymer fell from 2000 to 800. The process in argon slowed down as the polymer was "sewn up" and lost solubility during degradation (Fig. 7).

Degradation in oxygen exhibits more complicated kinetics. After formation of a three-dimensional structure and complete loss of solubility the process accelerates, owing to exothermic reactions involving oxygen and the contribution of the thermomechanical degradation of stressed structures. Polydiphenylamine remains completely soluble in polar solvents on the initial, non-stationary section, while its molecular weight increases to 6000–8000. After this, as the start of accelerated breakdown is approached, the solubility of the polymer diminishes rapidly.

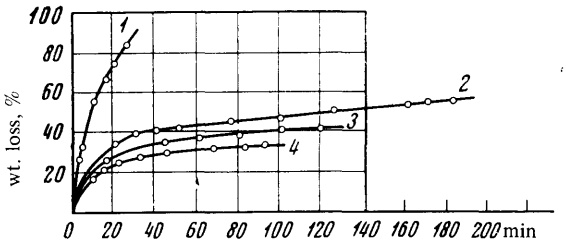


Figure 5. Thermo-oxidative degradation at 300°C and 1 atm of a thermolysed resite: 1) "freshly thermolysed" resite; 2) resite after 12 h in oxygen; 3) resite after 36 h in oxygen; 4) phenol containing the resite.

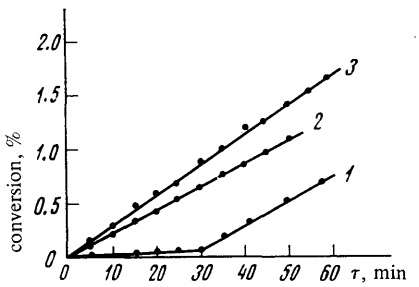


Figure 6. Catalytic activity, in the polymerisation of methyl methacrylate, of a thermolysed resite after exposure to air for (min): 1) 60; 2) 30; 3) 10.

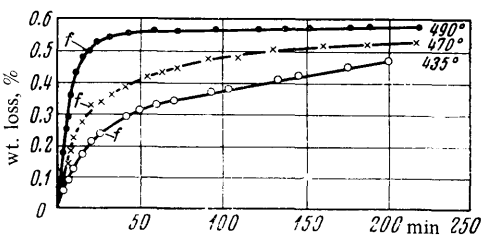


Figure 7. Weight losses in the thermal degradation of polydiphenylamine ($\overline{M}_n$ = 820) in argon.

Analysis showed that the main gaseous products of the degradation of polydiphenylamine in air were carbon and nitrogen dioxides. Degradation evidently begins with addition of an oxygen molecule at a double bond in the quinonimine structure and formation of a cyclic peroxide, which decomposes with the evolution of nitrogen dioxide.

Kinetic data indicate that the concentration of paramagnetic centres increases during the initial stages of degradation in air, then decreases, and again begins to rise almost simultaneously with the appreciable increase in rate of decomposition (Fig. 8). The variation in the concentration of paramagnetic centres in argon resembles the corresponding weight-loss curves [26].

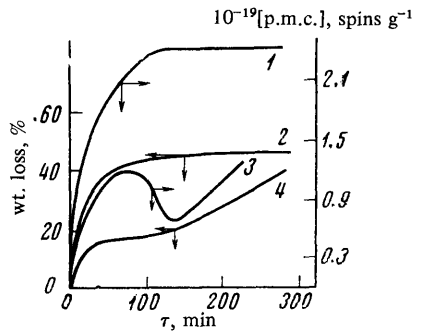


Figure 8. Variation in concentration of paramagnetic centres [p.m.c.] and weight losses in the thermolysis and thermal oxidation of polydiphenylamine: 1) [p.m.c.] in argon at 490°C; 2) loss in weight in argon at 490°C; 3) [p.m.c.] in air at 412°C (the polymer loses solubility and fusibility at the point of inflexion); 4) loss in weight in air at 412°C (as for curve *3*).

If a specimen is first heat-treated in argon until solubility is lost, and then placed in oxygen, the concentration of paramagnetic centres in the polymer falls rapidly, while its rate of decomposition increases autocatalytically. Preliminary thermal oxidation, on the other hand, improves the thermal stability of the polymer (Fig. 9).

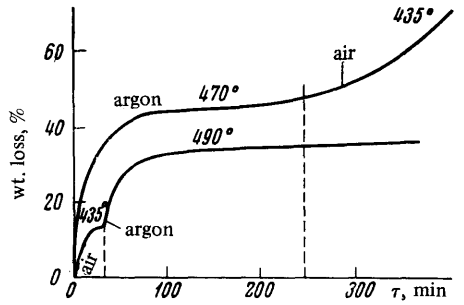


Figure 9. Rate of loss in weight when polydiphenylamine is heated in argon and in air.

This rule is probably explained by the increased concentration of active radicals trapped in the thermolysis of polydiphenylamine and their destruction ("burning out") in the preliminary thermal oxidation of the polymer. The broadening of the e.s.r. signal with the appearance of a fine structure indicates that the centres formed differ in nature from those in the original polymer associated with low-lying triplet levels. Condensation takes place more rapidly in oxygen, and the time for formation of a completely cross-linked structure is shortened. In the initial stages of formation of the network the paramagnetic centres are able to react with active radicals and be used up. As the structure becomes more rigid the rate of formation of new active radicals (by the rupture of stressed bonds) rises, and the concentration of paramagnetic centres reaches a limiting value.

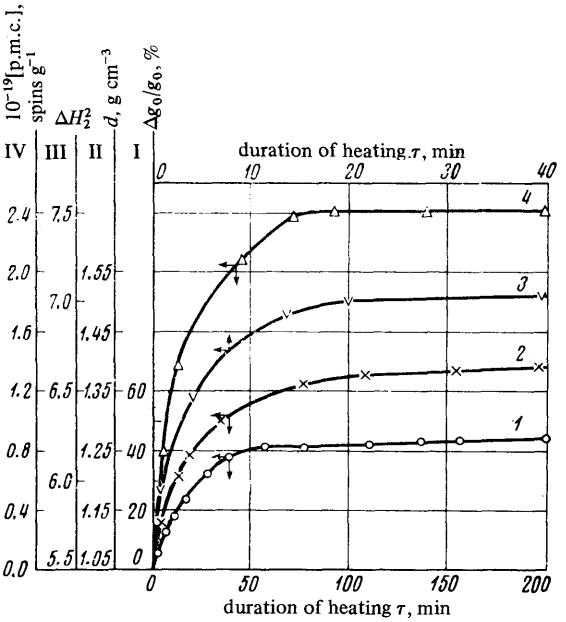


Figure 10. Rate of loss in weight and change in properties of thermolysate of polydiphenylamine ($\overline{M}_n$ = 2000) in argon at 470°C: 1) loss in weight; 2) density; 3) second magnetic moment of n.m.r. spectra; 4) concentration of paramagnetic centres from e.s.r. data.

The correctness of the above ideas can be confirmed by data indicating a correlation of the rate of thermal degradation of polydiphenylamine with the rate of increase in density, the increase in the concentration of paramagnetic centres, and the decrease in the molecular mobility of the polymer during its heat-treatment (Fig.10).

The limitation of the degradation curve of polydiphenylamine under isothermal conditions, which is general for polyconjugated systems [20,21], coincides with the completion (under the given conditions) of rearrangement of the polymer structure and formation of more thermostable fragments of fused aromatic rings. This process may be repeated with rise in temperature, which is responsible for the stepwise form of the weight-loss curves.

Thus the presence of oxygen should help to "burn-out" the most stressed portions with the formation of more

stable structures. Fig. 9 shows that preliminary treatment of polydiphenylamine in air at 435°C improves significantly its thermal stability in argon at 490°C, whereas heat-treatment of the polymer in argon diminishes its thermo-oxidative stability. In the latter case the structure formed on heat-treatment contains reaction centres, which in an oxygen atmosphere are able to react even during the formation of the network.

The whole of the above discussion indicates that the active centres produced in the thermolysis of cross-linked polymers act as initiators. Formation of the thermolysates probably involves relaxation processes leading to a decrease in the active surface area and partial destruction of paramagnetic centres. The presence in the polymer of substances of low molecular weight, capable of reacting with the radicals formed and exerting a plasticising action, enhances the probability of destruction of the radicals that have "stuck", and this improves the thermo-oxidative stability of the polyconjugated polymer [22-24].

Thus trivial considerations of the "cage" effect as a factor inhibiting a chain process cannot be used to describe the high-temperature degradation of rigid cross-linked and polyconjugated systems. The above results must be taken into account in developing methods for the synthesis and stabilisation of thermostable organic polymers.

III. SYNTHETIC PATHS TO THERMOSTABLE ORGANIC POLYMERS

When considering the formation of macromolecules of polyconjugated polymers, we must take into account the great tendency of these substances to form stable association complexes by intermolecular exchange interaction of unpaired electrons delocalised along the conjugated chain and π-electrons of multiple bonds [6]. In the absence of steric hindrance, therefore, chain growth in such macromolecules is accompanied by their aggregation and consequent impairment of the solubility of the resulting polymer. A direct consequence of this is diminished accessibility of reactive groups to the reagent and a change in their reactivity owing to resonance stabilisation caused by intra- and inter-molecular delocalisation of π-electrons [3,6]. The above specific features of the formation of polyconjugated macromolecules make it difficult to obtain polymers of high molecular weight and to process them into various goods and materials. This gives rise to difficulties in synthesising soluble or fusible conjugated oligomers and high polymers, capable of conversion into three-dimensionally cross-linked, parquet, and ladder polymers at the processing stage. These difficulties can be overcome by the use of reagents yielding polyconjugated macromolecules having side chains or groups that prevent dense packing of the chains. Methods based on the synthesis of polyconjugated systems containing polar and in particular ionogenic groups, responsible for specific solvation and solubility of the polymer in polar media, are also gaining importance.

Polyconjugated systems of high molecular weight (e.g. polyheteroarylenes) are often obtained also by a two-stage method involving the formation of soluble polymers, in which π-electron delocalisation is confined to small structural units, with subsequent conversion into polyconjugated systems by intramolecular reactions.

In view of the tendency of polyconjugated molecules to associate, which impedes or excludes their processing as solutions or melts, conversion of a high polymer into a polyconjugated system during synthesis may be advisable if the structure of the macromolecules of the resulting polyconjugated high polymer is unfavourable to their dense packing. Thus the problem of the controlled synthesis of highly thermostable organic polymers capable of being processed can be solved only if the specific structure and properties of polyconjugated polymers are taken into account. The considerable progress made in this field supports the principle that the study of polymers having a developed system of π-electron conjugation forms the scientific foundation for highly thermostable polymers.

The above specific aspects of the formation and structure of polyconjugated systems suggest the following main routes for the synthesis of oligomers and high polymers suitable for service at high temperatures and subject to radiation.

1. Synthesis of soluble and fusible oligomers with a polyconjugated system and the development of methods for their conversion into three-dimensional or planar network structures without significant disturbance of polyconjugation or the creation of molecular defects. Attainment of this aim requires the presence in the macromolecules of side-groups preventing dense packing but able under conditions of thermolysis (or radioysis) to bind macromolecules without any appreciable contribution of degradtive processes causing weight losses, increased contraction, and stresses.

2. Preparation of soluble compounds of high molecular weight with valency saturated chains and containing groups necessary for the formation of polyconjugated systems by intramolecular cyclisation and elimination, and in several cases structural units with π-electron conjugation. A polymer suitable for processing can be obtained at the synthesis stage only if the macromolecules contain either substituents that prevent dense packing or ionogenic groups.

3. Discovery of methods for synthesising block copolymers containing various polyconjugated fragments or connecting portions of "saturated" and of polyconjugated structure. Block copolymers containing organometallic blocks and fragments of π-electron (e.g. aromatic) polyconjugation may become especially important. In the last case not only plastics but also elastomers combining high thermal stability with strength may be obtained.

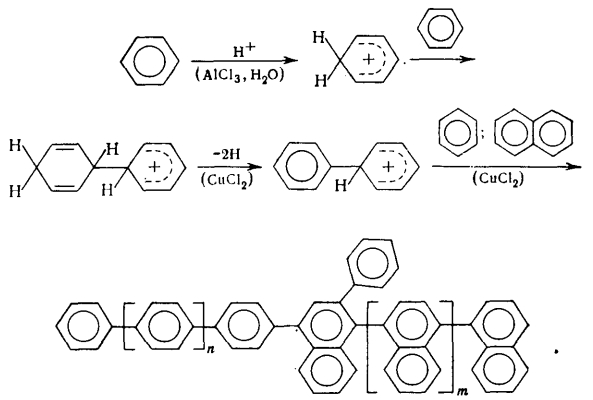
1. Polyconjugated Oligomers

Soluble oligomers suitable for the production of thermostable network polymers have been successfully synthesised in the cases of polyconjugated systems containing aromatic or heterocyclic rings joined either directly or through heteroatoms (polyheteroarylenes).

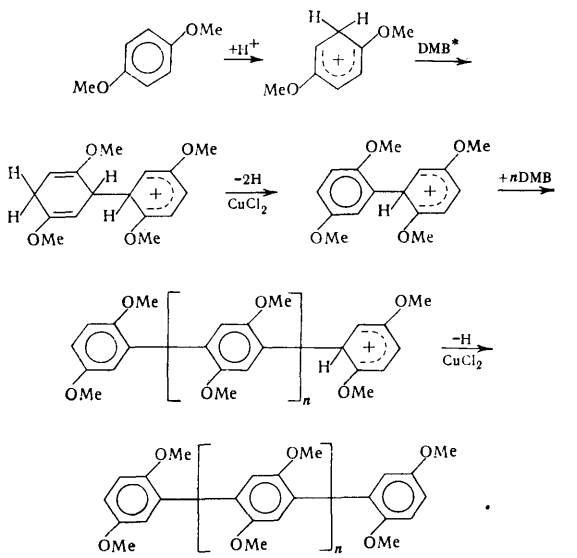
Among polyconjugated carbon-chain compounds, special interest attaches to branched oligoarylenes [27-29] and ladder oligomers of disubstituted buta-1,3-diyne [30-33]. Soluble and fusible (up to 250–400°C) oligoarylenes ($\overline{M}_n$ = 1000–3000) have been obtained by the cationic dehydrocopolycondensation of benzene with aromatic hydrocarbons in the presence of Lewis acids and dehydrogenating agents [copper(II) chloride, nitrobenzene, etc.].

The impossibility of synthesising high-molecular-weight polyarylenes in the melt and in solution is probably due to the above inactivation, characteristic of polyconjugated systems, of the reaction centre in donor–acceptor complexes formed by the growing polymer chains. Soluble and fusible polymers of naphthalene and anthracene, their

copolymers with benzene [27,28], and also polymers and copolymers of bi- and ter-phenyls [29], possess thermochemical stability in air up to 500 and in an inert gas up to 900°C. The probable mechanism of the oxidative polycondensation of aromatic hydrocarbons can be represented by a scheme analogous to that of Kovačic [34]:



Polycondensation in the presence of oxidants and Lewis acids has recently been extended to quinol and its derivatives, which has led to the synthesis of soluble oligoquinones and oligoalkoxyphenylenes having $\overline{M}_n$ = 1000 to 1500:



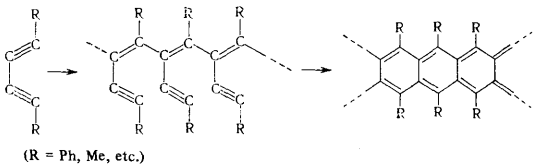
*p-dimethoxybenzene

Such polymers are stable in air up to 350°C, and are of considerable interest for the preparation of thermostable plastics and electron-exchange materials of high capacity (9–17 mg-equiv. g^{-1}). [35]

Various modifications of the Wurtz–Fittig, Ullmann, and several other reactions have been used to prepare soluble polyarylenes from aromatic monomers containing phenyl, methyl, and nitro-substituents [3,14].

A promising route to oligoarylenes suitable for processing is the high-temperature (340–450°C) dehydropolycondensation of acenes and their derivatives in the presence of conjugated paramagnetic polymers, which serve as activators. The soluble oligoanthracene obtained in this way is superior in thermal stability to the analogue synthesised by the use of Lewis acids [36,37].

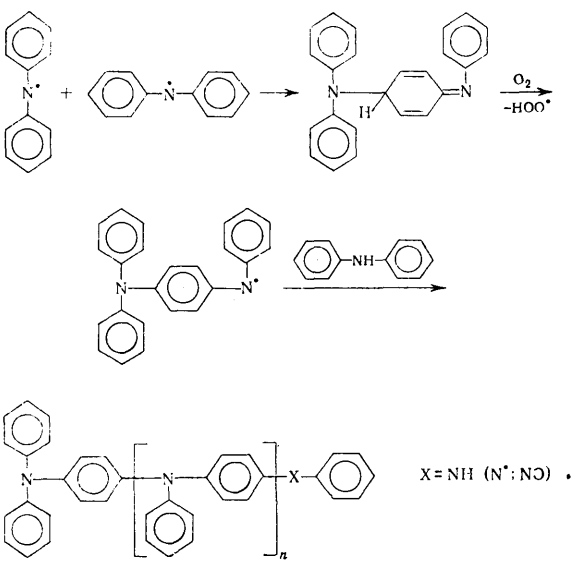
The synthesis of soluble polyconjuated oligomers having a ladder structure is of considerable interest. Such substances have been obtained by the thermal (195–400°C) and the catalytic [with $(C_4H_9)_3Al$ + $TiCl_3$ at 50–70°C] polymerisation of 1,4-diphenyl- and 1,4-dimethyl-buta-1,3-diynes [30–32]:



(R = Ph, Me, etc.)

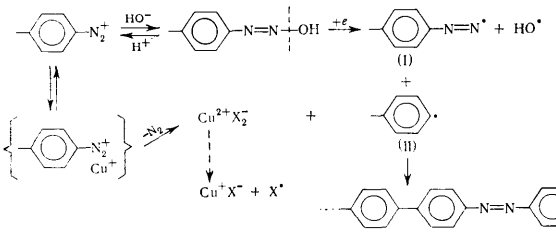
A ladder oligodiphenylbutadiyne having $\overline{M}_n$ = 3000–5000 dissolves readily in aromatic hydrocarbons, chloroform, dioxan, etc. Treatment of films of cyclised oligodiphenylbutadiyne at 1000–3000°C was accompanied by relatively small (15–35%) weight losses and yielded carbon having a graphitic structure. The electrical conductivity of the products at 300°C was 1.7–15 ohm^{-1} cm^{-1}, and the activation energy of conduction 0.04–0.06 eV. Products of the high-temperature treatment of oligodiphenylbutadiyne did not lose weight when heated in air to 700°C.

The oxidative polycondensation of secondary aromatic amines opens up interesting potentialities for the directed synthesis of polyconjugated systems [38–40]. It has been established experimentally that the oxidation of amines by oxygen in the melt at 200–250°C yields soluble, fusible oligomers of $\overline{M}_n$ = 1500–3000, possessing high thermochemical stability (temperature of progressive decomposition 450–500°C) and able to inhibit the thermo-oxidative and radiation degradation of carbocyclic and heterocyclic polymers. Available data suggest that polyarylenepolyamines are formed by the scheme

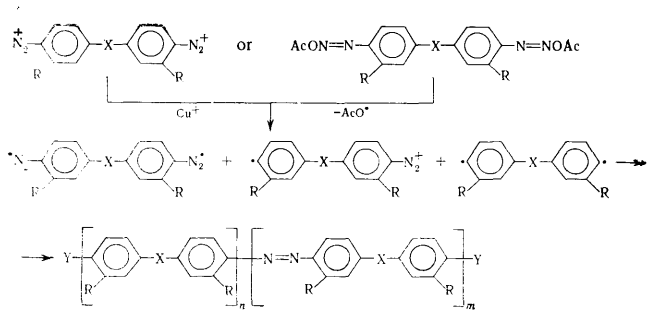


The polydeazotisation of aromatic bisdiazonium salts and bisnitrosoacylamines [41,42] shows great promise for the synthesis of soluble and fusible polyconjugated oligomers. This reaction is an example of non-equilibrium polycondensation by a radical mechanism. The deamination of

aromatic bisdiazonium salts in the presence of reductants probably has the mechanism [42,43]



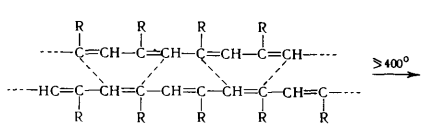
Interaction of radical centres of the growing chain with chloride ions in the redox reaction complex leads to chain termination. This liberates an electron, which is captured by the oxidised copper cation. Chain growth can cease only by conversion of the end of the growing polymer molecule into an inactive, stable radical having a considerable proportion of quinonoid structure. The content of combined nitrogen in the resulting oligomers varies with their structure from 1–2% to 7–8%. Bisdiazonium salts or bisnitrosoacylamines containing loosening phenyl, alkyl, or ionogenic groups in the aromatic ring must be used to obtain soluble oligoazoarylenes of $\bar{M}_n$ = 4000–8000:

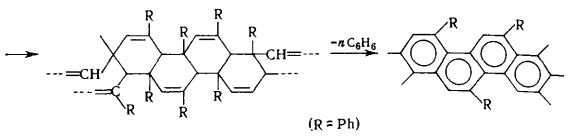


where X represents O, S, CH_2, or a single bond and R = H, Alk, Ar, COOH, OH, SO_3H, NO_2, or NHCOR.

Oligoazoarylenes are similar to oligophenylenes or the corresponding oligoarylenes in thermochemical stability [41,49]. Surprisingly, the elementary composition of oligoazoarylenes varies little when they are heated to 500–700°C, and azo-groups conjugated with benzene rings are preserved in the oligomer up to 700–1000°C. Polydeazotisation can be used to obtain oligoheteroarylenes containing metallocene groups [44]. Such polymers possess high thermochemical stability in an inert atmosphere (up to 700–800°C), but in the presence of oxygen they are degraded at 350°C.

The possibility of improving the thermal stability while maintaining solubility by appropriate heat-treatment of polyconjugated oligomers containing loosening fragments is based on controlling the fragments of a fused aromatic containing loosening groups [23,32,45]. Thus heating polyphenyl(phenoxy or pyridyl)acetylenes at 350–400°C for a short time ($1\frac{1}{2}$–2 h) converts them into soluble, dark-coloured oligomers containing fused aromatic structures [22,32]. This involves degradation with partial elimination of side radicals: e.g. in the thermolysis of polyphenylacetylene





the loss in weight at 400°C is 50% (H_2, C_6H_6, and $C_{12}H_{10}$ are eliminated), and the resulting black polymer retains solubility and possesses higher thermal stability (Fig. 11), electrical conductivity [2,45], and concentration of paramagnetic centres (the last by 10^3) than the initial polymer.

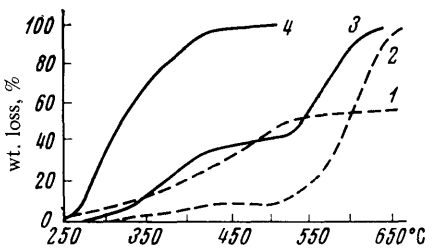
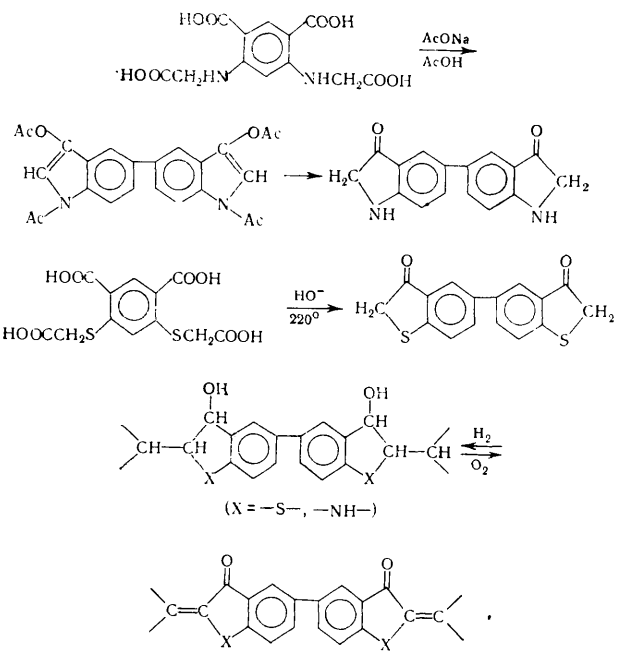
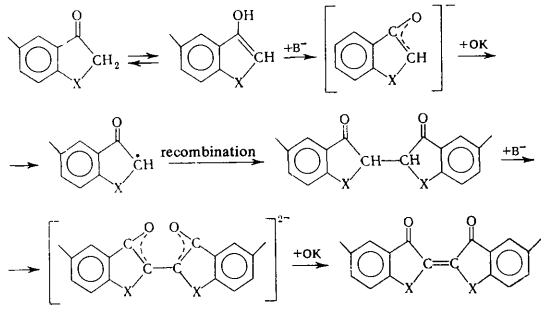


Figure 11. Thermal and thermo-oxidative degradation of soluble polyphenylacetylenes prepared in: 1) vacuum at 400°C; 2) presence of oxygen at 400°C; 3) presence of oxygen at 150°C; 4) vacuum at 150°C. At point *a* the polymer loses its fusibility and solubility [cf. Figs. 3 and 8].

The recently developed principle of the reversible conversion of insoluble into soluble polymers by redox reactions in polyconjugated oligomers and polymers [46,47] is also acquiring great importance. This method is analogous to vat dyeing, and the first "vat polymers" have been polyindigoids. Polyindigo and polythioindigo have been synthesised by oxidative polycondensation [42,46,47]



Electron spin resonance spectra obtained during the process and investigation of the products formed by termination of the growing chains on a stable radical (1,1-diphenyl-2-picrylhydrazyl) suggest the mechanism



B = base; OK = oxidant (O_2; etc.)

for the oxidative polymerisation of indoxyl and its analogues [42].

Polyindigo and polythioindigo are oligomeric polyconjugated systems of $\overline{M}_n = 4000$ possessing the magnetic and semiconducting properties usual for substances of this type. Polymeric indigoids (especially polythioindigo) also exhibit high thermal stability (up to 400–500°C) and are easily reduced by dithionite to the leuco-form, which is soluble in alkaline aqueous solution. Oxidation of the leuco-form in air yields polyindigo again. These transitions are reversible [42]. Vat dyeing with polymeric indigoids improves the thermal stability and the strength of several synthetic fibres (Fig. 12). Polyindigoids are promising also for obtaining heat-resistant coatings and as resins possessing electron-exchange and catalytic properties.

In connection with the above it is becoming urgently necessary to seek new synthetic routes to soluble oligomeric homo- and hetero-arylenes, e.g. oligoarylenazomethines [45,48], oligoarylenacetylenes [50,51], and several other polyconjugated oligomers.

2. Conversion of Polyconjugated Oligomers into Network Polymers

The transition from polyconjugated oligomers to polymeric materials and articles requires the development of rational methods permitting the conversion, at the processing stage, of fusible compositions into thermostable products possessing a specified set of physicomechanical properties. We shall now consider processes that have been suggested for "hardening" polyconjugated systems.

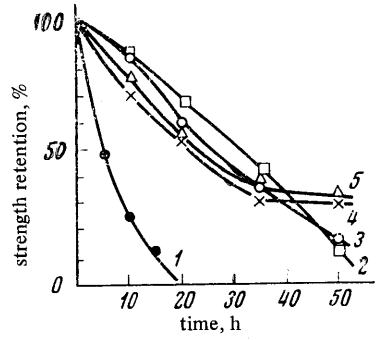
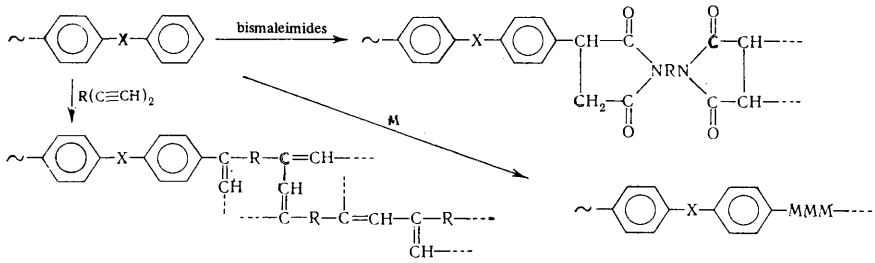


Figure 12. Strength of fibre based on a bicyclic lactam and caprolactam in air at 200°C after stabilisation with: 1) control; 2) thioindigo; 3) indigo; 4) polythioindigo; 5) polyindigo.

(*a*) Interaction of polyconjugated oligomers with compounds containing multiple bonds

Polyarylphenylenes, polyarylenes, and polyheteroarylenes containing paramagnetic centres have been shown in a series of studies [52–56] to be capable of spontaneous three-dimensional block copolymerisation at 150–200°C with *p*-diethynylbenzene and with bismaleimides of aromatic diamines or their analogues ("quasi-radical block polymerisation"). The polyconjugated oligomers containing paramagnetic centres initiate polymerisation of the electron-accepting monomers [25,54,56,57]:



X = $-C_6H_4-$, $-N{=}N-$, $>CO$, $>SO_2$, etc.; R = arylene; M = monomer

The discovery of this reaction, specific to polyconjugated systems, permitted the synthesis of thermostable soluble and three-dimensionally cross-linked block copolymers. The systems of compatible polyconjugated polymer and monomer (in several cases the latter was the solvent) were so chosen that compositions based on them possessed fluidity at the high temperature required to form the article. It is especially noteworthy that the "hardening" of a composition by quasi-radical block copolymerisation does not require the use of special

catalysts and is not accompanied by separation of products of low molecular weight, which might complicate the processing technology and impair the properties of the material.

The mechanism of quasi-radical block copolymerisation has been investigated on the systems formed by polyphenylacetylene with maleic anhydride and with methyl metacrylate[56-58]. Nuclear magnetic resonance shows that the first step is formation of a charge-transfer complex between the polyconjugated oligomer and the monomer:

$$P\uparrow\!---\!\downarrow P \overset{K_e}{\rightleftarrows} P\uparrow + M \overset{K_1}{\rightleftarrows} [P\uparrow\!---M]$$
(donor-acceptor complex)

where P↑---↓P represents associated polyphenylene macromolecules containing paramagnetic centres (the symbol ↑ denotes the presence of unpaired electrons), M a monomer molecule, and P the polyconjugated polymer. The complex [P↑---M] can be formed only if polyconjugated system and monomer are densely "packed" and if the electrophilic character of the latter is enhanced. Under otherwise similar conditions, therefore, the π-complex formation that limits polymerisation will depend on the structure and the configuration of the polyconjugated system and the monomer. The reaction is most probably initiated by thermal excitation of the reactants to a biradical state, followed by isomerisation to monoradicals, which carry on the chain polymerisation in contact with the surface of particles of the polyconjugated system. Formation of a block copolymer is evidently a consequence of termination or transfer of the growing chain. Such a mechanism can be represented to a first approximation by the scheme

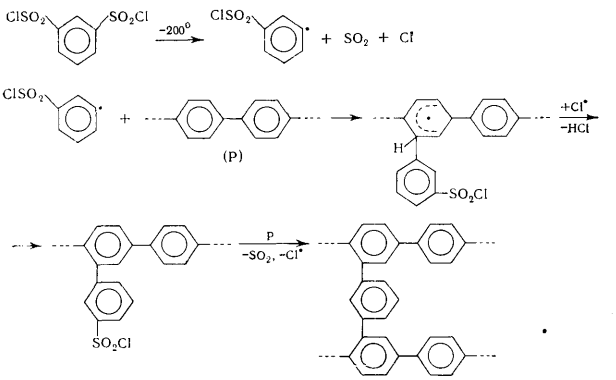
$$[P\uparrow\!---M] \overset{+M(k_i)}{\rightleftarrows} [P\uparrow\!---M\!---M] \xrightarrow{E(k_t)} [P\uparrow\!---M_1\!---M_2]$$
$$[P\uparrow\!---M_1] \xrightarrow{+M(k_p)} [P\uparrow\!---M_1MMM^{\cdot}] \xrightarrow{+M_nMMM^{\cdot}(k_t)} P\uparrow + [M]_n$$
$$P\uparrow + MMMM \overset{k't}{\rightarrow} P\uparrow - MMMM \ .$$

According to this scheme, raising the temperature and conducting the reaction in a homogeneous melt or solution should increase the yield of the block copolymer. When an insoluble polymeric polyconjugated system is used as catalyst, e.g. the pyrolysate of a phenol–formaldehyde resite[25,59], and the process is carried out at a moderate temperature ($\leq 100°C$), a stereoregular homopolymer is formed. It follows also from the scheme that the reaction velocity should be proportional to the concentration of the polyconjugated system raised to a degree $n < 1$ and to that of the monomer raised to a degree $n > 1$. All these suggestions showed good agreement with experiment[29].

The use of soluble and fusible compositions of polyarylenes with various cross-linking agents as binders for plastics reinforced with carbon or asbestos fibres will yield thermostable materials suitable for prolonged service at 300–350°C.[20] Such polymer systems are promising also for the production of thermostable coatings and adhesives.

(*b*) Formation of networks in polyconjugated oligomers by radical substitution

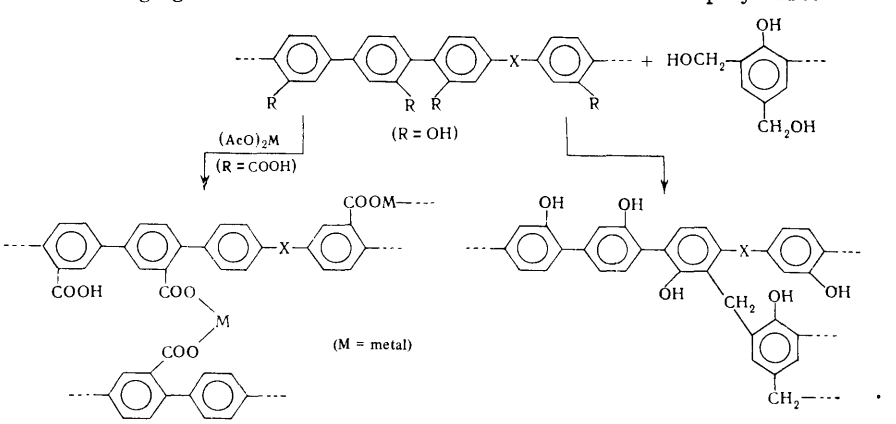
This method is based on the interaction of polyconjugated systems with aryl radicals formed by the high-temperature (150–200°C) degradation of aromatic disulphonyl dichlorides and certain other compounds:



Among the many possible cross-linking agents benzene-*m*- and *p*-disulphonyl dichlorides have acquired practical importance[60]. This reaction has recently been proposed for the synthesis of oligophenylene ($\overline{M}_n = 1775$), which can then be cross-linked or processed[61]. The reaction is accompanied by chlorination and the separation of by-products, which in several cases makes processing difficult and the method less promising than quasi-radical block copolymerisation. Nevertheless, high-strength asbestos and carbon plastics have been obtained by the use of benzenedisulphonyl dichlorides with additional heat-treatment[60,61].

(*c*) Conversion of polyconjugated oligomers into three-dimensionally cross-linked polymers by reactions of functional groups

Polyphenylenes and polyazophenylenes containing hydroxyl or carboxyl react with hydroxymethyl derivatives of phenols, phenol–formaldehyde resols, epoxide oligomers, metal salts, etc. to form infusible thermostable "cross-linked" polymers:



This method of "hardening" polyconjugated polymer systems has certain advantages over radical substitution (e.g. absence of chemically aggressive reaction products), but requires the presence of functional groups in the polyconjugated macromolecules. Known methods for the synthesis of carbon-chain oligomers depend on the use of aromatic or hydroaromatic hydrocarbons as starting material. Their conversion into polymers capable of being "hardened" by interaction with the above condensing agents requires the introduction of hydroxy-,[61] carboxy-,[2] or amino-groups into the aromatic rings.

In this connection considerable interest attaches to the polydeazotisation of aromatic bisdiazonium salts described earlier, which enables us to pass directly to oligoarylenes and oligoheteroarylenes containing almost any functional groups in the polyconjugated macromolecules, and to convert them into various types of network polymers[2,42].

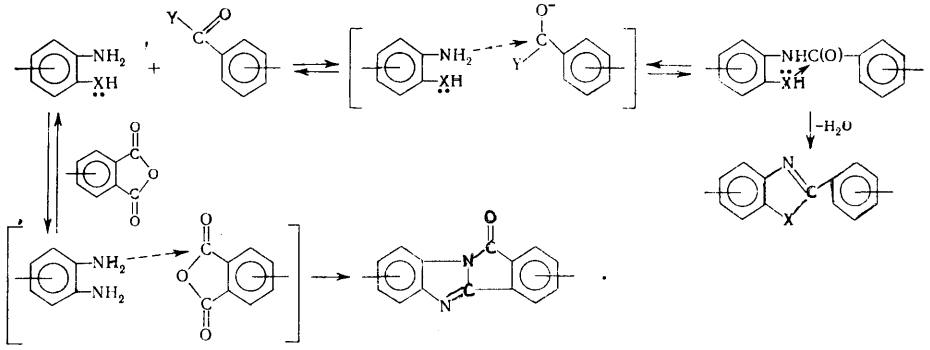
3. Synthesis of Polyconjugated Polymers of High Molecular Weight

The chemistry of polyconjugated polymers indicates that polyconjugated systems of high molecular weight can be produced only when difficulties in the growth of chains of continuous polyconjugation have been overcome. This can be achieved when there is maximum exclusion of π-electron delocalisation through large fragments of the macromolecules at the stage of chain growth, since only then are the possibilities of intermolecular aggregation and inactivation of the reaction centre diminished (see earlier). When the aim is to obtain a soluble high-molecular polyconjugated substance, it is also necessary to design the macromolecules to contain loosening groups or variegated fragments preventing dense packing of the chains.

These problems are solved most simple for "saturated" high polymers, capable of passing into polyconjugated systems by intramolecular detachment[2,18]. Examples of such processes are the thermo-oxidative dehydration of polysaccharides, dehydrocyclisation of polyacrylonitrile, dehydrochlorination of poly(vinyl chloride), and dehydration of poly(vinyl alcohol).

Considerably later (from 1960) an analogous method was applied to polycondensations yielding polypyromellitimide and several other polyheterocycloarylenes[63], and from 1966 to the synthesis of phenylated polyphenylenes[27,29]. Chain growth in the synthesis of polyheterocycloarylenes leads to the formation of compounds (e.g. polycarboxyamides, poly-*OO*-carboxyaminoamides) in which π-electron conjugation is confined to aromatic rings and groups attached directly to them. Polycondensation under mild conditions in a strongly polar medium at 20 to 70°C therefore yields initially chains of high molecular weight, which are then converted into polyconjugated high polymers by intramolecular cyclisation and detachment. Such conversion can be effected during synthesis or during subsequent processing of the prepolymer into articles.

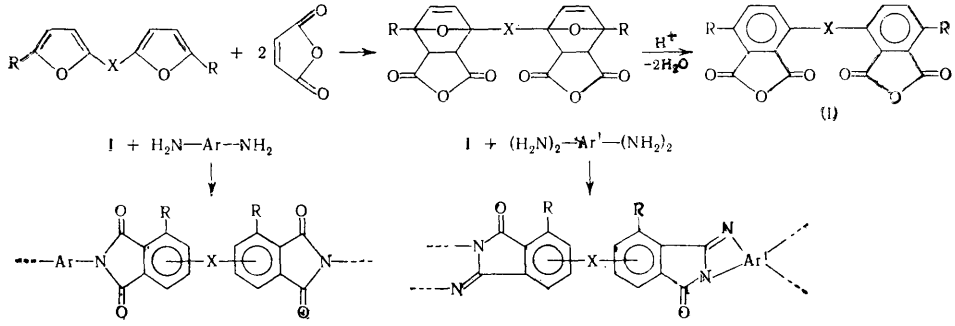
Loosening groups, e.g. phenyl, must be introduced into the chain in order to obtain soluble, almost completely cyclised polyheterocycloarylenes. Aromatic polyimides, polybenzimidazoles, polybenzoxazoles, polyimidazopyrrolones, polybenzimidazobenzophenanthrolines, polyquinoxalines, and many other polyheteroarylenes have been synthesised in this way[17,63]. The generality of the principle underlying the synthesis of high polymers having conjugated aromatic and heterocyclic ring systems is illustrated by the scheme



(X = NH, O, S, CONH, COO; Y = Cl, OR, CHO)

A promising line of advance in the field of polyheterocyclic polyconjugated systems is the synthesis of soluble polyimidazopyrrolones, polybenzimidazobenzophenanthrolines (pyrrones), and polyquinoxalines of semi-ladder, ladder, and block–ladder structure[1,17]. Solutions of pyrrones have been used to obtain strong and highly thermostable fibres, films, and foam plastics which are stable in an inert atmosphere up to 800°C and whose physicomechanical properties remain unchanged on irradiation with a dose of 10^4 Mrad.[16,17]

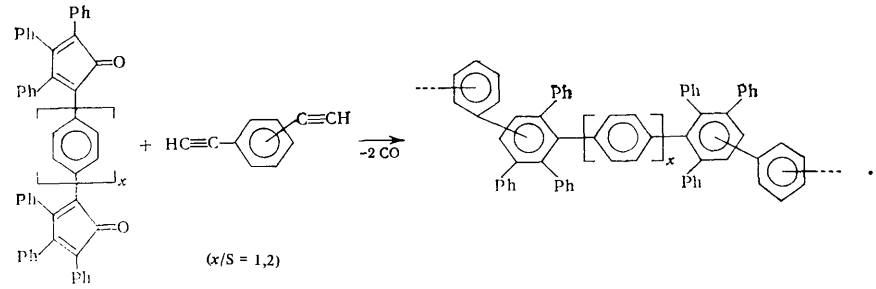
A recent advance of interest in developing the chemistry of polyheteroarylenes is the synthesis of polyimides and polyimidazopyrrolones from aromatised diadducts of maleic anhydride and various bisdienophilic compounds, e.g.[64]



(R = H, Ar; X = —CH=NArN=CH—; —Ar— —CH_2OOCArCOOCH_2—)

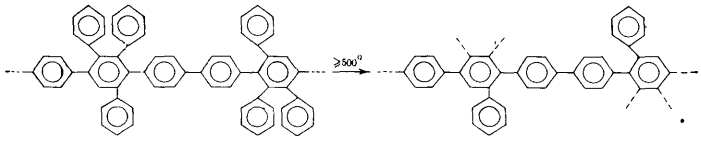
Investigation of the cyclopolycondensation of dianhydrides of tetracarboxylic acids with di- and tetra-amines has shown[64,65] that the most complete cyclisation is attained when the process is conducted as a single stage in polyphosphoric acid at 200–250°C. In the intramolecular cyclisation of the initially formed polyamino-acids and especially polyaminoamides the relative immobility of structural units in the chain evidently impedes the contact of reactant groups, which limits development of the conjugated chain and increases the proportion of weak bonds in the polymer. On the other hand, two-stage cyclopolycondensation is in practice unsuitable for obtaining thick articles, for cementing monolithic materials, or for producing reinforced plastics, since cyclisation occurs at a relatively high temperature and is accompanied by the evolution of volatile products. It is therefore very urgent to solve the problem of obtaining heterocyclochain polyconjugated systems that are soluble but yet of sufficiently high molecular weight. Polymers containing fragments that destroy the symmetry of the structure and diminish the density of packing of the macromolecules satisfy these conditions[6,63]. Interesting possibilities are opened up by the use of "reactant plasticisers" to facilitate the flow of pyrrones and their cross-linking during injection moulding and extrusion[66] and by the use of oligomeric analogues for the processing of pyrrones.

Aromatic carbocyclic–chain polyconjugated systems of high molecular weight have recently been acquiring increasing importance, as have the heterocyclic–chain type. Thus the polyaddition of diacetylenic aromatic hydrocarbons (e.g. *p*-diethynylbenzene) to bistetraphenylcyclopentadienones (tetracyclones) in toluene at 180–250°C gives a quantitative yield of a benzene-soluble, amorphous, weakly coloured polyphenylpolyphenylene[14]:



(x/S = 1,2)

The molecular weight of the phenylated polyphenylene is 20 000–100 000. In nitrogen at 575°C the polymer loses 30–35% of its weight, and passes into an insoluble brown product which in an inert environment is stable up to 800°C. This involves dephenylation and cross-linking[14]:



Paramagnetic centres appear in the polymer during heat-treatment and dephenylation, and its electrical conductivity increases.

The observed regularities are easily explained by the non-coplanarity of the aromatic rings in the polyphenylpolyphenylenes, which prevents conjugation from extending to more than two benzene rings. Favourable conditions are thereby created for the formation of a polymer of high molecular weight, which itself should not be regarded as thermostable. On thermolysis, however, the detachment of bulky groups changes the conformation of the chain with the appearance of a more coplanar polyconjugated polyphenylene; this is responsible for the thermal stability and other properties of the final material. Thus the example of phenylated polyphenylene bears an analogy to very many facts known for various polyheteroarylenes and heterocyclic–chain polymers.

Together with the data surveyed earlier, all this suggests that polyconjugation plays a decisive part in the formation of thermostable polymers and their subsequent transformations when subjected to powerful influences.

IV. ROLE OF POLYCONJUGATION IN THE THERMAL STABILITY OF POLYMERIC MATERIALS

We have come a long way and attained very considerable results during the fifteen years since the first publication establishing the concept of polyconjugation and its application to the synthesis of thermostable and semiconducting polymers [2]. The number of investigations inclined to accept these ideas and using them to develop rational methods for obtaining polymeric materials possessing high strength and thermal stability is now increasing [48,67,68].

However, several workers [69,70] approach the problem of the thermal stability of polymeric substances without taking into account intra- and inter-molecular π-electron delocalisation, i.e. in disregard of the main concepts of the chemistry and physics of polyconjugated systems. These investigators consider the difference in chemical nature between rings and other groups in the units, the configuration of the chains, and intermolecular interaction in the initial polymers. They completely ignore the role of π-electron delocalisation (conjugation) through fragments or through the chain of the macromolecules and its contribution to the intermolecular interaction and supermolecular structuring of polymeric substances. Further, they disregard the fact that the thermal stability of a material is determined in many cases not so much by the nature of the initial polymer as by the structure of the polymeric product formed by the action of thermal and other powerful factors. Yet, as shown above, it is electron delocalisation in the chains of the initial polymer and its thermal conversion products which determines the internal energy and the stability of the material under severe processing and service conditions.

It must be especially borne in mind that complicated chemical and structural changes take place in an organic polymer at high temperatures. These are responsible for (i) the growth of fragments of fused aromatic or heteroaromatic rings, with a consequent decrease in the internal energy and increase in the thermal stability of the system, and (ii) the associated increase in rigidity of the macromolecular chains and formation of three-dimensionally cross-linked polyconjugated structures. The latter processes (ii) are accompanied by increases in contraction and internal stresses, and they activate local thermal cracking of the most stressed bonds. Thus the chemical and structural changes observed in a polymer subjected to high temperatures are a prerequisite for the formation of reactive σ-radicals, as in mechanical degradation of macromolecular substances [71].

Further cross-linking with the accumulation of σ-radicals is probably the main reason for the poor stability of many cyclochain polymers under oxidising conditions at high temperatures. Thermal oxidation in such systems is initiated by reactions of σ-radicals, formed and "frozen" in the network, with oxygen at the surface of the specimen. The heat thus evolved activates neighbouring bonds and groups with the subsequent development of degradative processes. Owing to the restricted molecular mobility of the network, moreover, part of the heat evolved on interaction between oxygen and the radical cannot be dissipated in thermal lattice vibrations, and may be emitted as chemiluminescence [72], which also activates the development of thermal oxidation, as has recently been shown for the chemiluminescent initiation of polymerisation [73].

It is also possible that "hot" radicals [74] play a definite part in this process. The evolution of heat and the autocatalytic character of the high-temperature oxidation of rigid network polymers (polyconjugated systems) may be responsible for the observed thermal ignition of thermolysed resites [24]. This suggestion is supported by the above correlation of the increase in density and decrease in molecular mobility of the cross-linked thermolysate with increases in the degree of conversion and in the rate of thermal oxidation, and also by the catalysis of radical polymerisation by resite specimens that have been thermolysed at 450°C. The hypothesis is supported also by the loss of ignitability and catalytic activity which we have observed [24] after blocking of the active centres of these substances.

The views and experimental facts considered in this Review indicate that organic polymers with high resistance to thermal oxidation cannot be synthesised on the basis of rigid-chain, ladder, parquet, or network structures not containing fragments that increase the thermal mobility of the molecular framework. A directly opposite point of view is often adopted on this matter.

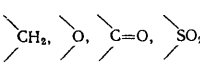
The concept of polyconjugation and the ideas underlying the chemistry and physics of polyconjugated systems are applicable also to aromatic carbon-chain and heterochain polymers. Such substances as phenol–formaldehyde resites, aromatic polyamides, polyimides, etc. are usually regarded as saturated polymers comprising aromatic rings separated by the particular groups. Such polymers surpass acyclic analogues in strength and thermal stability, and in several cases (polypyromellitimides) are closely similar to polyphenylenes and polycycloheteroarylenes containing large fragments of continuous conjugation. Hence it is deduced that the thermal stability of organic polymers is due to the presence of stable rings and the consequent rigidity of the macromolecular chains [14,69,70]. Such ideas hardly touch the essence of the phenomenon, although they reflect certain of its consequences.

Table 2. Polyconjugation in aromatic polyamides [75].

No.	Molecular structure	η_{sp}	Long-wavelength absorption λ_{max}, nm	10^{-15} [p.m.c.], spins g^{-1}
1	Benzanilide	—	276	**
2	Terephthalamide	—	304	**
3	*m*-Phenylenanilide	—	300	**
4	Poly-*m*-phenylenisophthalamide	0.88	280	4.6
5	Poly-*m*-phenyleneterephthalamide	0.58	300	8.2
6	Poly-*p*-phenylenisophthalamide	1.22	305	9.2
7	Poly-*p*-phenyleneterephthalamide	1.27	330	16.0
8	Poly-*p*-phenyleneterephthalamides differing in mol.wt.	0.04	314	2.2
9		0.14	318	5.6
10		0.35	330	12.3
11*		1.27	330	16.0
12*		1.27	330	24.6

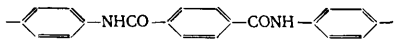
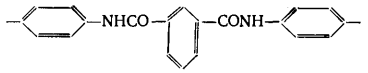
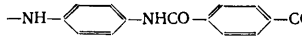
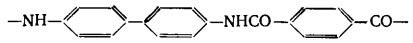
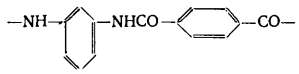
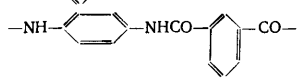
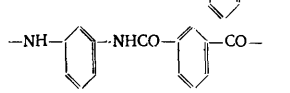
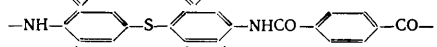
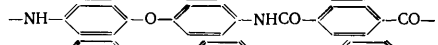
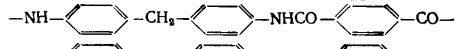
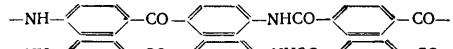
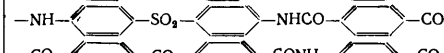
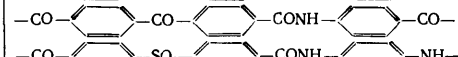
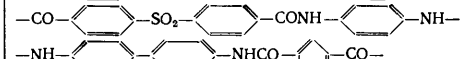
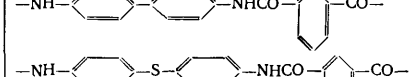
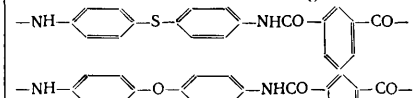
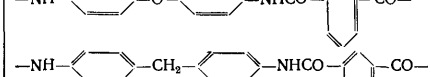
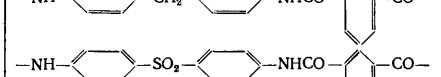
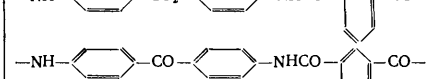
*Specimens 11 and 12 were obtained by precipitating polymer 7 from dilute solution in sulphuric acid (with water and ethylene glycol respectively). This considerably diminished the crystallinity of the polymer.
**Not detected.

Recent quantum-chemical and spectral investigations have shown that aromatic polyamides, polyimides, and other types of polyheteroarylenes are polyconjugated polymers [75]. The presence of the bridging groups



does not exclude π-electron delocalisation through extended fragments of the macromolecule[75]. Such polymers showed high π-electron exchange interactions along the chain, bathochromic shifts in the ultraviolet absorption spectra with increase in length of the macromolecule, and also the narrow e.s.r. singlet, with the g-factor of a free electron and becoming more intense with increase in molecular weight, that is characteristic of polyconjugated systems (Tables 2 and 3). The same work has established that the presence of *meta*-substituted aromatic units (e.g. in polyisophthalamides), like the presence of electron-accepting bridging groups in the amine component, diminishes the polyconjugation effect by changing the electron configuration of the molecules. All this is consistent with existing views on polyconjugation and on the properties of polyconjugated polymer systems[18,41,76].

Table 3. Long-wavelength absorption bands of various polyamides[75].

No.	Polyarylenamide	λ_{max}, nm
1		304
2		280
3		330
4		345
5		300
6		305
7		280
8		360
9		330
10		320
11		330
12		300
13		320
14		305
15		330
16		330
17		310
18		300
19		290
20		330

It is interesting that the thermal stability and several physical properties of aromatic polyamides and polyimides correlate with their effective conjugation, to which attention has been directed repeatedly[17,18,22]. The effect of polyconjugation may not be apparent in the initial state of polymers containing disconnected aromatic or heteroaromatic rings systems, as in several saturated acyclic polymers capable of eliminating groups when sufficiently stressed. Under various powerful influences, however, such systems are converted into polyconjugated systems with more or less substantial structuring and contraction, depending on the nature and structure of the polymers and the conditions of treatment.

We have thus directed attention to the role of polyconjugation—electron delocalisation through extended fragments of macromolecules and their association complexes—which in the Reviewer's opinion determines the thermal stability and other properties of polymers. This does not mean, of course, that the Reviewer denies the connection discussed in the literature between the structure of a unit, the presence of so called "weak bonds", and thermal stability, or the effect of chain rigidity on the resistance to degradation and the strength of polymers. However, none of this represents a foundation on which specific aspects of the degradation of highly thermostable polymers could be understood, and methods developed for their planned synthesis.

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Progress in the Search for Chemical Protective Agents against Radiation

V.G.Yashunskii

Information published during 1968–1973 on the search for protective agents, capable of preventing or diminishing the harmful action of ionising radiation, is discussed and analysed. Only synthetic monomers belonging to various classes of organic compounds are considered: the search for protective compositions is not discussed. The bibliography comprises 168 items.

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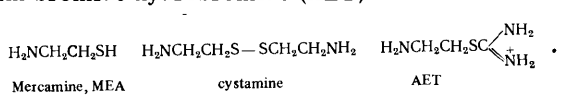
I. INTRODUCTION

A quarter of a century has elapsed since the first demonstration that chemical protection of animals from ionising radiation was possible[1,2]. During this period an immense amount of work has been done on synthesising and studying the prophylactic radiation-protective action of several thousands of synthetic and natural substances of diverse structure. Among them have been discovered extremely effective protective agents, capable under experimental conditions of preventing the death of a considerable proportion of animals subjected to X-rays and γ-rays. It can be concluded from the results that the living organism can in principle be protected by means of chemotherapeutic agents from ionising radiation, but considerable difficulties arise in applying such protection to man, since there is no proof that the doses of these agents that he can tolerate are able to protect him from the action of radiation. The whole 25-years' period of development can be arbitrarily divided into three stages.

The initial stage, from 1949 to the mid-1950s, saw the discovery of protection by chemicals and the start of the search for such agents among various classes of chemical compounds. The second stage, from the mid-1950s to 1968, extended the search for substances which would diminish radiation damage in animals, with a deeper study of compounds showing the greatest protective effect in experiments and attempts to bring the most effective of them to clinical application. An achievement of this stage was the production of such protective preparations as 2-aminoethanethiol (mercamine, MEA), the corresponding disulphide (cystamine), and *S*-2-aminoethylthiouronium bromide hydrobromide (AET)



However, the considerable toxicity and the narrow therapeutic spectrum of these products made it urgently necessary to find more efficient protective agents. By the end of the 1960s, after many different chemical compounds had been studied (~ 3000 by 1965), the impression was created that chemical protection from radiation was of only theoretical importance, and preparations better than the above three could not be obtained. It was even suggested that the whole idea of protection from ionising radiation by means of chemical substances was unpromising.

In this connection one of the pioneers of chemical protection (Bacq) wrote: "... a tendency has become evident to overlook the possibility that new protective chemicals might appear and to focus attention on studying the most active of known agents. However, it is not impossible that more active and far less toxic chemical protective agents will be discovered in the near future".[3] These words of Bacq's have proved to be prophetic: indeed, publication started to appear in 1968 which marked the beginning of the current stage in the development of chemical protection of the living organism from ionising radiation. This stage has seen considerable advances in the production of protective agents and, most importantly, the establishment of confidence in the reality of the practical application of chemical prophylactic radiation-protective agents. The number of substances that have been synthesised and studied as potential protectors has been rapidly increased by slight variations on the optimum chemical structures discovered previously. The main aim has been to find agents of great therapeutic spectrum; the results up to 1971 have been covered in brief reviews[4,5].

The present Review studies and analyses results, published from 1968 to 1973 inclusive, of the search for monomeric synthetic prophylactic protective agents. The greatest attention has been paid during this period, as in previous years, to the search among compounds based on the 2-aminoethanethiol structure. Interesting results have been obtained also for other sulphur-containing compounds and heterocycles.

Before the main subject of the Review is discussed, brief consideration must be given to the quantitative assessment of the efficiency of radiation-protective agents, a problem which has been faced repeatedly[3,6]. American authors[7] have suggested a "protective index"

$$I = \frac{LD_{50}}{ED}\left(1 + \frac{a}{100}\right),$$

representing both the degree of protection and the therapeutic spectrum for a given substance, where LD_{50} is the dose of the agent causing the death of 50% of the animals and a is the percentage survival of the animals with the given effective dose ED and complete mortality in a control group. This parameter has limited application,

since it permits comparison of the efficiencies of substances only under identical experimental conditions (mode of introduction, time of administering substance before irradiation, species of animal, dose and dosage rate of radiation, etc.). However, since the experimental conditions have been adequately standardised during recent years, the protective index can in many cases be used to estimate the practical prospects. Table 1 gives a scale of efficiencies of protective agents based on the protective index and adopted by several American authors.

Table 1. Scale of efficiency of protective agents.

I	0—1	2—5	6—10	11—44	⩾ 15
	0* ineffective	+ relatively ineffective	++ moderately efficient	+++ efficient	++++ highly efficient

* It is assumed that $I = 0$ when protection is below 20%.

The protective index will be used where possible in the present Review. Since the vast majority of experiments with protective agents have been made on mice with the substances introduced 15–30 min before irradiation at 40–400 rad min^{-1}, and the survival rate of the animals was determined after 30 days, these conditions may not be satisfied in the text of the Review.

II. SULPHUR-CONTAINING COMPOUNDS OF AMINOTHIOL STRUCTURE

Among the sulphur-containing compounds studied during the past five years as prophylactic protective agents the vast majority are *N*-substituted derivatives and analogues of 2-aminoethanethiol–thiols, disulphides, thiosulphates, thiophosphates, thiazolidines, etc.—as well as similar compounds in which the ethylene chain has been modified. A considerably smaller number of other sulphur-containing compounds have been studied. They will be discussed in this sequence.

1. *N*-Substituted 2-Aminoethanethiols

Although 2-aminoethanethiol itself has a fairly high protective effect under experimental conditions, its practical use is prevented by its narrow therapeutic latitude of action. With intraperitoneal (ip) injection LD_{50} = 250 mg kg^{-1}, and in the optimum dose ED = 150 mg kg^{-1} it protects 87% of mice when a control batch shows complete destruction; with oral (or) introduction LD_{50} = 615 mg kg^{-1}, ED = 300 mg kg^{-1}, and a = 73%: hence for mercamine

$$I_{ip} = \left(1 + \frac{87}{100}\right)\frac{250}{150} = 3.1,$$

$$I_{or} = \left(1 + \frac{73}{100}\right)\frac{615}{300} = 3.6.$$

On the above scale [Table 1] mercamine must be regarded as a relatively ineffective protective agent. Naturally, therefore, numerous attempts have been made in recent years to vary the structure of mercamine in every possible way in order to obtain a product with the same level of protection against radiation but with a greater latitude of action, i.e. one which is less toxic and better tolerated.

Earlier investigations on the effect of the anion on the protective activity of mercamine have been continued by a detailed examination of its adenosine triphosphate salt [9]. This agent, termed Tsitrifos, was closely similar to aminoethanethiol hydrochloride in activity, but exhibited a protective effect on prolonged irradiation at 10.7 and 3.75 rad min^{-1}.

Various workers have prepared and studied many derivatives of the type

$$RHNCH_2CH_2SH$$

(I)

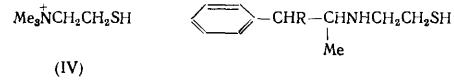
with different *N*-substituents, but most of them were relatively inactive or possessed a weak protective action. Replacing an amino-hydrogen atom by a straight- or branched-chain alkyl results in disappearance of the protective activity [10]. Compounds having a long normal alkyl chain (I: R = C_8H_{17}, C_9H_{19}, $C_{10}H_{21}$) exhibit a protective effect [11]. Polymethylene-*NN'*-bis-2-aminoethanethiol derivatives (II) containing n = 6–8 CH_2, [12] as well as their sulphone analogue (III), [13]

$$HSCH_2CH_2NH{-}A{-}HNCH_2CH_2SH$$

(II) A = $(CH_2)_n$ (III) A = SO_2

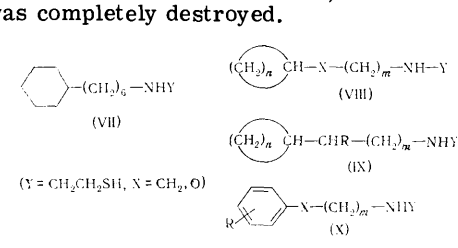
increase very slightly the radiation resistance of mice on prophylactic application. Quaternisation of the nitrogen atom produced a sharp increase in toxicity and a loss of activity, as has been observed with thiocholine (IV). [14]

$Me_3\overset{+}{N}CH_2CH_2SH$ (IV)



(V, R=H); (VI, R=OH)

Little or no protective effect is shown by aminoethanethiol derivatives containing alicyclic, aryl, and heterocyclic substituents attached to the nitrogen atom either directly or through 1–4 methylene groups [10,15]. Similar results were obtained in a study of *N*-substituted derivatives containing hydroxy-, alkoxy-, and aryloxy-alkyl substituents, and of aminoethanethiols with structures (V) and (VI) based on amphetamine and ephedrine [10]. Only one of the 58 such compounds examined in this work, 2-*N*-6'-cyclohexylhexylaminoethanethiol (VII), showed high protection against radiation: an intraperitoneal dose of 30 mg kg^{-1} given 15 min before irradiation provided almost complete protection for mice, whereas a control group was completely destroyed.



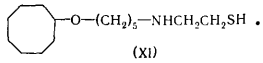
(VII) (Y = CH_2CH_2SH, X = CH_2, O)

(VIII) (IX) (X)

It was probably on the basis of these results that a group of investigators headed by Westland studied in 1972 [16] a series of compounds of type (VII) in which the substituent was an alicyclic ring (VIII) and (IX) or a benzene ring (X) attached by a polymethylene chain (C_3–C_6) either directly or through an oxygen atom to the amino-group, in some of which the polymethylene chain was branched (IX). Cycloalkylalkyl derivatives (VIII) were

considerably more toxic than aminoethanethiol itself and its closest analogues. Most of them, however, had a protective action in smaller doses (25–50 mg kg^{-1}, only 33–17% of the effective dose of 2-aminoethanethiol). Replacing a five-membered by a six-membered ring and varying the length of the polymethylene chain from three to six units had no significant effect on the protective activity of such compounds. Branching in the hydrocarbon chain leads to loss of or diminution in activity. The protective index of the most active does not exceed 3.5, which corresponds to the efficiency of aminoethanethiol itself.

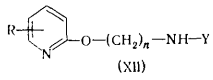
The sole exception among compounds of this type was the cyclo-octyloxypentyl derivative



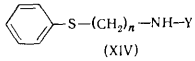
(XI)

While possessing considerably lower toxicity (LD_{50} = 180 mg kg^{-1}) than the other cycloalkylpolymethylene analogues, a 50 mg kg^{-1} dose of this compound protected 83% of mice when destruction in the control group was 100%, and its protective index I = 6.6.

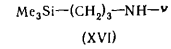
Aryloxyalkyl derivatives (X: X = O) were on the average rather more effective than their alicyclic analogues[16,17]. Among them compounds having n = 4–6 were the most active: the ethylene and trimethylene derivatives did not protect animals[13]. Increasing the number of alkyl substituents in the benzene ring diminishes the protective activity.



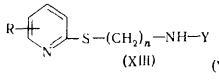
(XII)



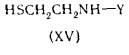
(XIV)



(XVI)

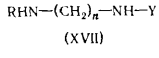


(XIII)



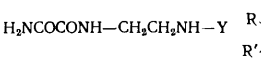
(XV)

(Y = CH_2CH_2SH)

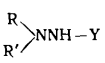


(XVII)

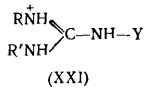
Among the 25 pyridyloxyalkyl derivatives of aminoethanethiol of type (XII) Westland and his coworkers[8] were unable to discover one which would have merited attention as a protective agent. Nor did the pyrid-2′-ylthioalkyl (XIII) and phenylthioalkyl (XIV) analogues, the N-mercaptoethyl (XV)[18] and N-trimethylsilylpropyl (XVI)[19] derivatives, possess a protective action.



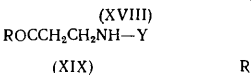
(XVIII)



(XX)



(XXI)



(XIX)

R = R′ = Me; R = H, R′ = C_8H_{17}

R = H, R′ = $PhCH_2CH$ (Me)

R = R′ = H, Me

Y = CH_2CH_2SH

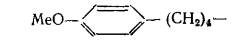
A few compounds have been studied whose alkyl substituent contains a secondary amino-group (XVII), but no active substance was discovered among them[20,21]. The oxamido-derivative (XVIII) had a slight protective effect[22]; replacing a hydrogen atom in the terminal carbamoyl group by phenyl, cyclohexyl, or pyridyl led to a loss of activity. A protective action was evident with derivatives containing a propionic acid residue attached to the amino-group (XIX)[21]; the most active was the amide (R = NH_2), which was followed by the acid (R = OH), the nitrile, and the ethyl ester (R = OC_2H_5). Replacing the amino-group in 2-aminoethanethiol by hydrazino (XX) leads to a loss of protective activity[10]. N'-Methylated derivatives (XXI) showed a considerably weaker protective action than did guanidinoethanethiol[24].

Thus in only one case, N-cyclo-octyloxypentylaminoethanethiol (XI) (I = 6.6), did the wide variation in the structure of the substituent attached to the nitrogen atom in 2-aminoethanethiol (~ 130 such compounds were studied) yield a considerably more effective protective agent.

(XXII, R=H) $(RNHCH_2CH_2S)_2$

(XXIII, R= –A

a A=CH(Me)$(CH_2)_3$–; b A=$CHCH_2$(Et),



(XXIV)

Aminoalkyl disulphides have aroused considerably less interest in investigators during recent years. The first member of this group, cystamine (XXII), while having several advantages over the corresponding amino-thiol (mercamine), must also be regarded as a relatively ineffective radiation-protective agent (with LD_{50} = 320 mg kg^{-1}, in the optimum dose (intraperitoneal) of 220 mg kg^{-1} it protects ~ 70% of mice[3]: i.e. I = 2.5). During the past 5–6 years great attention has been paid to the preparation and study of derivatives of (XXII) containing N-alkyl substituents substituted by cycloalkyl and cycloalkoxyl, aryl and aryloxyl, pyrid-2-yloxyl and quinol-2-yloxyl. Active compounds have been found among the cycloalkyl and aryl derivatives[13,16,17]; their heterocyclic analogues possessed no protective action[8]. The highest protective efficiency was found with bis-2-N-4′-cyclohexylpentylaminoethyl (XXIIIa)[16] and bis-2-N-4′-p-methoxyphenylbutylaminoethyl (XXIV)[17] disulphides, with the respective protective indices 8.4 and 11.0. It is interesting that the disulphide (XXIIIb), a close analogue of (XXIIIa) whose N-substituent differs by only one methylene unit, has no protective effect[16].

Table 2. Protective properties of amino-thiols and disulphides.

R	$RHNCH_2CH_2SH$				$(RHNCH_2CH_2S-)_2$				Ref.
	dose, mg kg^{-1}		protection, %	I	dose, mg kg^{-1}		protection, %	I	
	LD_{50}	ED			LD_{50}	ED			
cyclo-$C_6H_{11}CHMe-(CH_2)_3-$	75	50	17	0	45	10	85	8.4	16
cyclo-$C_6H_{10}O-(CH_2)_5-$	180	50	83	6.6	560	160	50	5.8	16
2,6-$Me_2C_6H_3O-(CH_2)_4-$	75	50	80	2.7	560	160	17	0	16
2,3,6-$Me_3C_6H_2O-(CH_2)_4-$	130	100	33	1.7	56	32	50	2.2	16
4-$MeOC_6H_4-(CH_2)_4-$	70	40	15	0	240	60	83	11.0	17
Br– –$O-(CH_2)_6-$	140	60	87	4.4	78	20	0	0	8

Table 2 reveals no regular variation in toxicity and protective activity on passing from an amino-thiol to the corresponding disulphide: either an increase or a decrease in toxicity, accompanied by an increase, a decrease, or maintenance of the protective activity, may be observed depending on the nature of the substituent.

Kostyukovskii et al.[14] found that increasing the degree of substitution of the amino-groups in cystamine leads to an increase in toxicity, while protection is maintained at the same level. Quaternisation of the nitrogen makes the compound extremely toxic and almost inactive.

$RR'NCH_2CH_2SH$ (XXV)

R = R′ = H; R = H, R′ = Me

$RR'NCH_2CH_2S-SCH_2CH_2NRR'$ (XXVI)

R = R′ = Me; R = H, R′ =

Tank and Zherebchenko[25] compared the toxicity and the protective activity of several thiol–disulphide pairs such as 2-aminoethanethiol (XXV) and cystamine (XXVI), and found that these properties vary with the species of animal. Thus with mice no relation could be established between the toxicity and antiradiation activity and the thiol or disulphide structure. Experiments on rats showed greater toxicity and a somewhat higher protective efficiency with disulphides than with the corresponding thiols.

$(AcNHCH_2CH_2S-)_2$ (XXVII)

$AcNH-(CH_2)_n-S-S-CH_2CH_2NHC_{10}H_{21}$ (XXVIII)

a $n=2$; b $n=3$

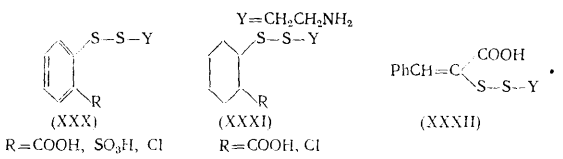
$AcNHCH_2CH_2-S-S-(CH_2)_4-X$ (XXIX)

a $X=SO_3Na$; b $X=SO_2Na$

Field and his coworkers[26-29] have made interesting investigations on the synthesis of symmetrical and unsymmetrical disulphides based on 2-aminoethanethiol and have studied their protective activity. It was discovered that *NN'*-diacetylcystamine (XXVII)[29], like its unsymmetrical analogue (XXVIIIa) having a long *N'*-alkyl substituent[26], does not protect mice from radiation. The homologue of the latter compound with three methylene units between the sulphur atom and the acetamido-group (XXVIIIb) showed a medium protective action[26].

The sulphonate (XXIXa) has a weak protective effect[27], whereas the corresponding sulphinate (XXIXb) proved to be an efficient protective agent. An intraperitoneal dose of the latter sodium salt of 172 mg kg^{-1} (LD_{50} = 800 mg kg^{-1}) protected 93% of mice when destruction of a control group was complete (I_{ip} = 9.0). The degree of protection given by oral introduction of (XXIXb) was also high: a dose of 278 mg kg^{-1} with LD_{50} = 1050 mg kg^{-1} gave 100% survival of the animals (I_{or} = 7.5).

Substances having protective properties have been discovered also among unsymmetrical disulphides of the types[28]

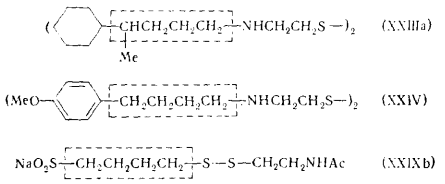


(XXX) R=COOH, SO_3H, Cl

(XXXI) R=COOH, Cl

(XXXII)

It is extremely interesting that the most active disulphides



* Presumably these formulae had originally been numbered (XXXIII)–(XXXV) (Ed. of Translation).

are structurally similar, for they all contain a chain of four carbon atoms. Unfortunately, the lack of data do not allow a reason to be suggested for the role of this factor in the protective effect.

Although less interest has evidently been taken during recent years in disulphides as potential protective agents than in the amino-thiols from which they are derived (a total of ~ 45 such compounds have been studied), highly efficient products have been discovered among them, such as bis-2-*N*-4'-*p*-methoxyphenylbutylaminoethyl disulphide (XXIV) and sodium 4-2'-acetamidoethyldithiobutanesulphinate (XXIXb), the latter showing considerable effectiveness when administered orally. This suggests that the potentialities of 2-aminoethyl disulphides as protective agents are by no means exhausted, and that still more efficient products may be expected to appear in this series.

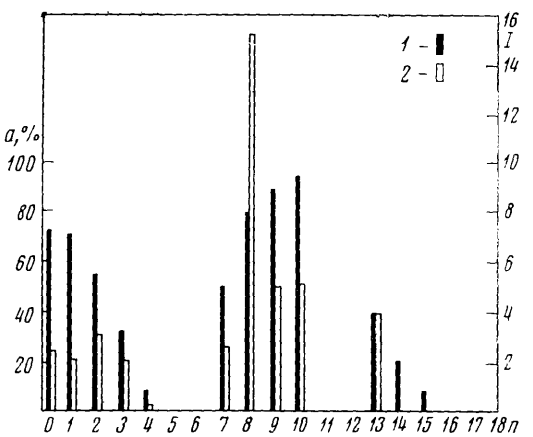
2. *N*-Substituted Aminoethyl Thiosulphates (Bunte's Salts)

In the search for protective agents containing the 2-aminoethanethiol structure the greatest attention has been paid during the past five years to derivatives of aminoethyl thiosulphates, Bunte's salts. The discovery in 1968 of extremely high protective action among these compounds[7] was in effect a turning point in the search for chemical means of protection from ionising radiation.

$H_3\overset{+}{N}CH_2CH_2SSO_3^-$ (XXXVI)

$R\overset{+}{N}H_2CH_2CH_2SSO_3^-$ (XXXVII)

The primogenitor of this series of compounds—2-aminoethyl thiosulphate (XXXVI)—possesses a high protective effect, but in doses which are almost toxic[30]. With LD_{50} = 450 mg kg^{-1} the optimum protective effect of 73% survival was observed with an intraperitoneal dose of 350 mg kg^{-1} in mice. Thus I = 2.2 for (XXXVI): i.e. the compound is relatively inefficient.



Effect of number n of carbon atoms in alkyl group in the compounds $C_nH_{2n+1}N^+H_2.CH_2.CH_2.SSO_3^-$ on: 1) percentage survival of mice a; 2) protective index I.[31]

Klayman et al.[31] studied the prophylactic protective action against radiation of many *N*-alkylated aminoethyl thiosulphates (XXXVII), and discovered an interesting relation between the protective effect and the size of the alkyl group, clearly illustrated by the diagram. Three peaks of activity can be seen, and it is interesting that activity does not always vary in parallel with toxicity. Several Bunte salts containing branched-chain alkyls attached to the nitrogen atom have quite a high protective effect. This is most clearly shown by the 1-methylheptyl derivative (XXXVIII), which in a dose of 75 mg kg^{-1} protects all animals from an absolutely lethal dose of radiation (I_{ip} = 3.7). Among the more than 30 *N*-alkylated

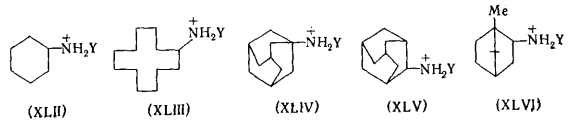
derivatives (XXXVII) studied the most effective protective agent was *N*-octylaminoethyl thiosulphate (XXXIX): at a dosage of 15 mg kg^{-1} with LD_{50} = 125 mg kg^{-1} (intraperitoneal) the survival rate of mice was 80% (I_{ip} = 15.0). Another compound of this series, decylaminoethyl thiosulphate, showed a protective action of ~ 50% at doses of 10–30 mg kg^{-1} in monkeys [32].

$Y{=}CH_2CH_2SSO_3^-$ $C_6H_{13}CH(Me)-\overset{+}{N}H_2-Y$ (XXXVIII) $n-C_8H_{17}-\overset{+}{N}H_2-Y$ (XXXIX)

The encouraging results obtained in the study of *N*-alkylated aminoethyl thiosulphates stimulated an intense search for protective agents among various *N*-substituted derivatives and other amino-thiol compounds. Polymethylene-*NN'*-bisaminoethyl bisthiosulphates (XL) were relatively inactive [12]. A quite well defined protective action was shown by certain compounds containing higher hydroxyalkyl and methoxyalkyl groups (XLI). [7]

$Y{=}CH_2CH_2SSO_3^-$; $Y-\overset{+}{N}H_2-(CH_2)_n-\overset{+}{N}H_2-Y$ (XL), n=6–9; $RO-(CH_2)_n-\overset{+}{N}H_2-Y$ (XLI), R=H, Me; n=4, 7–10

Several workers [7,15,16] have studied the protective properties of Bunte salts having alicyclic substituents in the amino-group. The antiradiation activity of compounds in which the alicyclic substituent is attached directly to the nitrogen atom depends on the size of the ring and the bulk of the substituent. Thus the cyclohexyl derivative (XLII) is inactive [7], whereas the cyclododecyl analogue (XLIII) possesses a moderate protective action [15]; the 1- and 2-adamantyl (XLIV) and (XLV) and the 2-bornyl (XLVI) derivatives are considerably more active [15].



(XLII) (XLIII) (XLIV) (XLV) (XLVI)

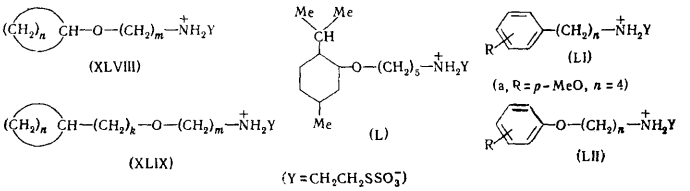
($Y = CH_2CH_2SSO_3^-$)

It was shown for cyclopentane and cyclohexane derivatives that introducing a polymethylene chain between the alicyclic substituent and the nitrogen atom leads to the appearance or enhancement of activity with a diminution in toxicity [7]. The optimum length was pentamethylene. Activity was found among compounds containing four-, five-, six-, and seven-membered rings.

It is interesting that, in a series of derivatives with straight-chain alkyl substituents, maximum efficiency is found with the C_8 group, whereas in cycloalkylalkyl derivatives this occurs in most cases when the substituent contains a total of nine or ten carbon atoms. Branching in the hydrocarbon chain joining the alicycle to the amino-group improves the efficiency of the protective action while having diverse effects on the level of toxicity, as is shown by Table 3 for cyclohexylalkyl derivatives (XLVII). [7]

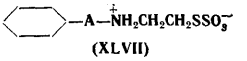
It is worth noting that Westland et al. reported [16] that the *L*-form of *N*-cyclohexylbutylaminoethyl thiosulphate (XLVIIa), while possessing the same toxicity as the racemate, is almost trebly efficient as a protective agent. The laevorotatory isomer has the very high protective index I_{ip} = 30.

Analogues of the above compounds containing an ethereal oxygen atom between the alicycle and the hydrocarbon chain (XLVIII) or in the chain itself (XLIX) also have a protective action against radiation [7,16]. Among them (XLVIII: n = 7; m = 4) [7] and 5'-*L*-menth-3''-yloxypentylaminoethyl thiosulphate (L) [16] are distinguished by their activity, with protective indices I_{ip} of 9.0 and 8.0 respectively.



(XLVIII) (XLIX) (L) ($Y = CH_2CH_2SSO_3^-$) (LI) (a, R = *p*-MeO, n = 4) (LII)

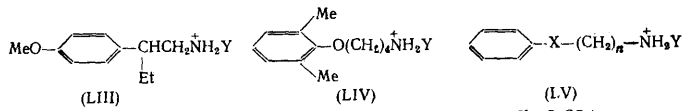
Table 3. Protective properties of cyclohexylalkyl derivatives.



(XLVII)

A	LD_{50}, mmole kg^{-1}	ED, mmole kg^{-1}	Protection, %	I
CH_2	1.36	0.43	20	0
$(CH_2)_2$	0.34	0.19	27	2.3
$(CH_2)_3$	0.58	0.39	86	2.8
$(CH_2)_4$	0.17	0.034	87	9.4
$(CH_2)_5$	0.03	0.015	7	0
$(CH_2)_6$	0.028	0.014	53	3.2
$CHMeCH_2$	0.43	0.18	40	3.4
$CHEtCH_2$ (a) (racemate)	1.00	0.17	80	10.8
$CH(Me)-CH_2CH_2CH_2$	0.25	0.08	100	6.3
$CH(Et)-CH_2CH_2-$	0.48	0.08	60	9.6
$CH_2CH(Et)-CH_2$	0.45	0.048	73	16.3

Equally detailed studies have been made on *N*-arylalkyl (LI) and *N*-aryloxyalkyl (LII) derivatives of aminoethyl thiosulphate [7,17,33]. Among the former type (LI) the most active were the mono- and bis-methoxyphenyl derivatives having n = 4 or 5, and the greatest attention has been attracted to *N*-4'-*p*-methoxyphenylbutylaminoethyl thiosulphate (LIa). A dose of 30 mg kg^{-1} with LD_{50} = 120 mg kg^{-1} gave 87% protection to mice, whereas a control group underwent complete destruction (I_{ip} = 7.5). It is interesting that its isomer (LIII) with the same branched chain as in the most active cyclohexane analogue (XLVIIa) was inactive [17]. Introducing an ethereal oxygen atom between the benzene ring and the polymethylene chain has no significant effect on the toxicity or the protective action of the compounds. The nature of the substituent in the benzene ring is also almost without effect on the activity. Branching in the chain removes the protective action.

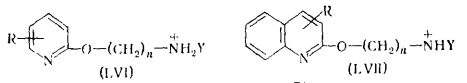


(LIII) (LIV) ($Y{=}CH_2CH_2SSO_3^-$) (LV) (X=S, SO_2)

The most efficient protective agent of this series of compounds is 2''',6'''-dimethylphenoxybutylaminoethyl thiosulphate (LIV). With LD_{50} = 250 mg kg^{-1} a dose of 100 mg kg^{-1} provides 100% protection for mice, and a dose of 25 mg kg^{-1} gives 73% protection. The protective index is I_{ip} = 17.3.

Analogues (LV) of the above compounds in which a sulphur atom or a sulphonyl group has replaced the oxygen

atom in the chain exhibited no appreciable protective action[13].



(LVI) (LVII)

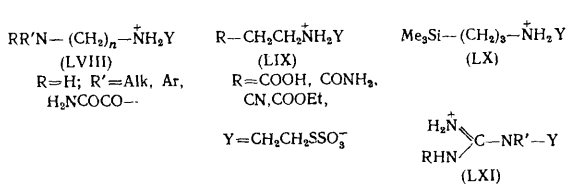
(Y = $CH_2CH_2SSO_3^-$)

Heterocyclic analogues of cycloalkoxy- and aryloxy-alkylated derivatives containing a pyridine (LVI) or a quinoline (LVII) ring have also been synthesised, and their protective action has been studied[8]. The former contained as substituents R halogen, nitro, and cyano at positions 3‴, 5‴, and 6‴, with the number of methylene units varying from 2 to 7. The quinoline derivatives contained methyl, trifluoromethyl, methoxyl, and chlorine in the ring, with 2–6 methylene units. Highly efficient protective agents having a large therapeutic spectrum of action were discovered among compounds of this type (Table 4).

Table 4. Protective properties of pyridine and quinoline derivatives.

Compound	R	n	Dose, mg kg^{-1}		Survival, %	I_{ip}
			LD_{50}	ED		
LVI	5-Br	4	180	100	93	
				50	60	5.8
LVI	5-Br	5	90	25	73	6.2
LVI	5-Cl	5	225	19	87	20.0
LVI	5-Cl	6	120	30	67	6.7
LVI	3,5-Br_2	5	163	25	67	11.0
LVII	H	3	220	25	93	17.0
LVII	4-Me	3	180	25	80	13.4
LVII	4-Me	4	225	50	93	8.7
LVII	6-MeO,4-Me	2	100	12	73	14.4
LVII	4.6-Me_2	3	125	19	93	12.7

By analogy with the thiol derivatives, studies were made on several Bunte salts with an aminoalkyl chain attached to the nitrogen atom (LVIII) and containing the terminal amino-group either unsubstituted[34] or with aryl[20], oxamide[22], or other[21] substituent. However, none of them protected mice from radiation. Several derivatives of 2-aminoethyl thiosulphate containing a propionic-acid residue attached to the nitrogen atom (LIX) were studied[23] and all found to exhibit a weak protective effect against radiation. The trimethylsilylpropyl derivative (LX) was also inactive[19]. Klayman et al.[35] examined several derivatives of guanidylethyl thiosulphate of type (LXI), and found most of them to possess a pronounced protective action. The most active was the derivative in which the nitrogen atoms were unsubstituted (LXI: R = R′ = H): a dose of 100 mg kg^{-1} (LD_{50} = 275 mg kg^{-1}) protected 80% of mice: I_{ip} = 5.0.



(LVIII) R=H; R′=Alk, Ar, H_2NCOCO–

(LIX) R=COOH, $CONH_2$, CN, COOEt,

Y=$CH_2CH_2SSO_3^-$

(LX)

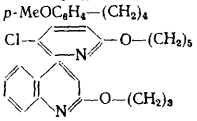
(LXI)

It had been thought earlier that derivatives of aminoethyl thiosulphate had no protective action on mice when given orally. Westland et al.[7,17] disputed this opinion, having discovered moderate activity on the oral introduction of several of the above *N*-cycloalkyl- and *N*-arylalkylated derivatives showing the greatest protective effect on intraperitoneal administration. Oral introduction diminished the toxicity of these compounds by 90–99%, but considerably larger doses were required to achieve a protective effect.

Among the above compounds *N*-*p*-methoxyphenylbutylaminoethyl thiosulphate (LIa) showed the greatest protective action. When introduced 30 min before irradiation, it protected up to 87% of mice; shortening the period to 15 min led to a sharp decrease in the survival of the animals.

The above experimental results for ~ 300 aminoethyl thiosulphate derivatives as protective agents administered intraperitoneally lead to certain conclusions on the effects of the structure of the *N*-substituents on toxicity and protective activity. Alkyl and cycloalkyl-, aryl-, and heteryl-alkyl substituents, in several cases with some increase in toxicity, led to an appreciable decrease in the protective dose and thereby widened the therapeutic spectrum. The optimum structure in this series must evidently be regarded as that in which the *N*-substituent in the aminoethyl thiosulphate contains 8–12 carbon atoms, one or two of which may be replaced by nitrogen or oxygen atoms. If the substituent is not purely aliphatic, the number of methylene groups joining the cyclic fragment to the amino-group should be 3–5.

Table 5. Protective properties of R–$N^+H_2CH_2CH_2SSO_3^-$.

R	Doses				I_{ip}	Ref.
	LD_{50},		Ed,			
	mmoles kg^{-1}	rel. to XXXVI	mmoles kg^{-1}	rel. to XXXVI		
H (XXXVI)	2.9	1	2.2	1	2.2	30
n-C_8H_{17}	0.46	0.16	0.056	0.025	15.0	31
cyclo-C_6H_{11}–CH (Et) * – $(CH_2)_2$	1.00	0.36	0.060	0.027	30.0	16
p-$MeOC_6H_4$–$(CH_2)_4$	0.77	0.25	0.093	0.042	7.5	17
	0.64	0.22	0.053	0.024	20.0	8
	0.65	0.22	0.047	0.021	17.0	8

* *L*(–)-isomer.

Table 5 gives comparative data for the most efficient protective agents—*N*-substituted aminoethyl thiosulphates—which clearly demonstrate the advantage of these compounds over their primogenitor—2-aminoethyl thiosulphate itself. The protective efficiency of such compounds is evidently determined not so much by the length of the group, which may influence the surface-active properties of the compounds, as by the "weight" of the substituent (around 100–200), its configuration, and other factors. The broadened therapeutic latitude in these substances must be attributed to "dilution of the active fragment" by the increase in molecular weight. Table 5 shows that introducing a substituent increases the toxicity by factors 3–6 but at the same time diminishes the effective protective dose to a still greater extent, by factors of 20–40.

3. Derivatives of *S*-2-Aminoethyl Dihydrogen Phosphorothiolate

The first member of this series—*S*-2-aminoethyl dihydrogen thiophosphate (LXII)—whose sodium salt has since been termed Cystaphos, was first described in 1961 as an effective protection against radiation[36]. Cystaphos and its simple derivatives were shown to possess quite low toxicity while being highly active[36,37]. Thus with LD_{50} = 930 mg kg^{-1} Cystaphos itself in a dose of 400 mg kg^{-1} protects 95% of mice from an absolutely lethal dose of radiation[36]: i.e. its I_{ip} = 4.5. These were high values for the 1960s, and this series of compounds might have been expected to engross the attention of research workers. However, the literature indicates that fewer aminoethyl thiophosphates than thiosulphates and even thiols have been studied during the past five or six years as potential protection against radiation.

$H_2NCH_2CH_2SPO_3H_2$ (LXII) $RHNCH_2CH_2SPO_3H_2$ (LXIII)

The further search in this series for more efficient protective agents than Cystaphos was directed at complicating the molecule by introducing various hydrocarbon and other groups at the nitrogen atom. Most of the compounds synthesised were isolated and used as the sodium and other salts (formulae in the text will be given for the dihydrogen esters). More than 40 compounds of type (LXIII) have been described containing various substituents—alkyl, carboxyalkyl, carbamoylalkyl, etc.[38]—but data are not given on their protective activity against radiation.

$Y=CH_2CH_2SPO_3H_2$

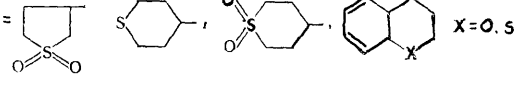
$YHN-(CH_2)_n-NHY$ (LXIV), n=7–10

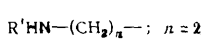
$YHN-(CH_2)_n-C_6H_{10}-(CH_2)_n-NHY$ (LXV), n=0,1

Some activity has been found with the polymethylenebisaminoethyl bisthiophosphoric esters (LXIV) and their *cis*- and *trans*-cyclohexane analogues (LXV).[12] Replacing an amino-hydrogen atom by bornyl and norbornyl groups diminishes the protective effect found in Cystaphos[15]. The adamant-1-yl derivative (LXVI), although more toxic, gave protection in a smaller dose: with LD_{50} = 560 mg kg^{-1} a dose of 80 mg kg^{-1} showed a protective effect of ~ 80% (I_{ip} = 12.5).[15] Weak protection or none at all was shown by compounds having a heterocyclic *N*-substituent (LXVII)[15] and by the *N*-phenoxy-, *N*-phenylthio-, and *N*-phenylsulphonyl-alkylaminoethyl esters (LXVIII)[13].

$R-HNCH_2CH_2SPO_3H_2$

(LXVI) R =

(LXVII) R =  X=O, S

(LXVIII) R =  $X-(CH_2)_n-$, X = O, S, SO_2; n = 2, 3

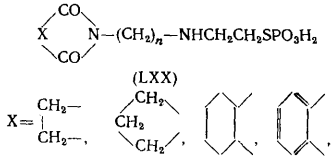
(LXIX) $R = R'HN-(CH_2)_n-$; n = 2–6

Attention was directed mainly at seeking protective agents among *N*-aminoalkyl derivatives of the *S*-aminoethyl thiophosphate (LXIX)[20,21,34]. Introduction of an aminoalkyl chain of 2–6 units terminating in a free amino-group (R′ = H) produces a significant increase in protective efficiency above that of Cystaphos[34]. All *N*-aminoalkyl derivatives other than the first member of the series (LXIX: R′ = H, n = 2) are more toxic than Cystaphos but protect animals in considerably smaller doses. Table 6 shows that most of them have protective indices exceeding that of Cystaphos by about 50%. The protective activity of certain compounds of type (LXIX) is maintained when a hydrogen atom of the terminal amino-group is replaced by methyl or ethyl (R′ = CH_3, C_2H_5); the introduction of an octyl or a cyclohexyl substituent (R′ = C_8H_{17}, C_6H_{11}) deprives the compound of activity[20]. The *N*-aminopropylaminoethyl ester (LXIX: R′ = H, n = 3)—known by the number WR-2721 or the name Gammafos—has been subjected to a more thorough and detailed study as a potential protective agent[39–42]. These investigations enabled the advantage of this agent over Cystaphos to be shown up more boldly.

Table 6. Protective properties of derivatives of (LXIX).

LXIX R′	n	Doses, mg kg^{-1}		Protection, %	I_{ip}
		LD_{50}	ED		
Cystaphos		930	400	95	4.5
H	2	1300	400	100	6.5
H	3	700	300	86	4.3
H	4	800	200	80	7.2
H	5	550	150	100	7.3
H	6	550	150	93	7.1
Me	3	800	200	87	
			100	46	11.7

Various *N*-imidoalkyl derivatives of the aminoethyl ester (LXX) (formed from the imides of succinic, glutaric, cyclohexane-1,2-dicarboxylic, and phthalic acids) have been studied in the search for more effective compounds[21,43,44]. Most of these compounds showed weak or moderate action against radiation. The most active was the cyclohexane derivative, which gave protection even when administered through the mouth[44].



(LXX)

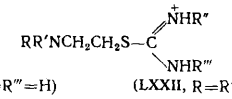
X = n=2–4

The above discussion can be summed up in the conclusion that, among the > 100 *N*-substituted aminoethyl dihydrogen thiophosphates described during the past six years, the most effective protective agents were the adamant-1′-yl (LXVI) and methylaminopropyl (LXIX: R′ = CH_3, n = 3) derivatives, with protective indices reaching ~ 12.

4. Aminoethylthiouronium Derivatives

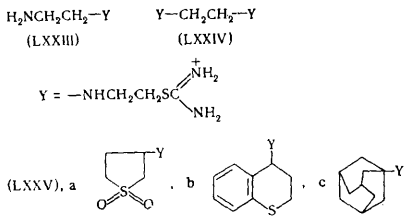
The search for protective agents has been considerably less intense among aminoethylthiouronium derivatives (LXXI), which, while possessing a high protective action, is itself an extremely toxic substance (I = 1.5–2.0). Japanese workers[45,46] examined systematically all possible

N-methyl derivatives (LXXII), but gave no data on their biological activity.

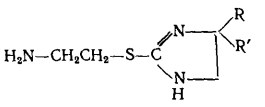


(LXXI, R=R′=R″=R‴=H) (LXXII, R=R′=R″=R‴=Me, H)

The aminoethyl derivatives (LXXIII) and (LXXIV) are inferior in protective activity[47] to the original aminoethylthiouronium.



Elliott and his coworkers[15] discovered that derivatives of (LXXI) having heterocyclic residues such as dioxothiophanyl and thiachromanyl attached to the chain nitrogen atom (LXXVa, b) possess no protective activity, whereas the adamant-1′-yl analogue (LXXVc) develops some action.



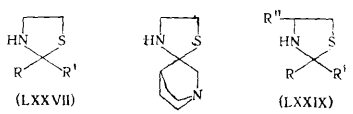
(LXXVI)

(R=R′=H; R=R′= Alk, cycloAlk)

Derivatives of (LXXI) have been synthesised with amino-acid and dipeptide residues in the thiouronium group[48], but, like the cyclic analogue (LXXVI)[47,49], these compounds were inferior to aminoethylthiouronium itself in protective activity against radiation.

5. Thiazolidines

Increasing interest has been taken during recent years in thiazolidines, cyclic analogues of 2-aminoethanethiol. The search for protective agents was continued in the traditional direction—among 2-substituted thiazolidines (LXXVII), which are usually regarded as a long lasting, less toxic form of aminoethanethiol because of their ability to break down gradually in the organism with liberation of the latter product. Among compounds of this type studied, several exhibited moderate protective activity—unsubstituted thiazolidine (LXXVIIa), the 2-alkyl and 2-aryl[50], also the 2,2-dimethyl (LXXVIIb) and 2-trichloromethyl (LXXVIIc) derivatives[51], and 2,2-spiroquinuclidylthiazolidine (LXXVIII)[52].

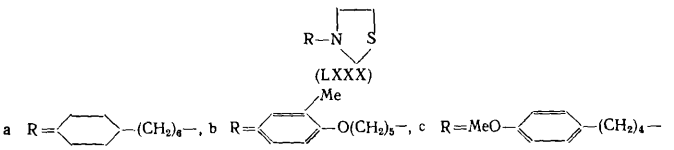


(LXXVII) (LXXVIII) (LXXIX)

a R=R′=H;
b R=R′=Me;
c R=H, R′=CCl_3;
d R=Me, Pr, Ph; R′=COOEt;
e R=Me, Pr, Ph; R′=CH(CH_2Ph)COOEt

a R=R″=H, R′=COOR‴ (R‴=H, C_1-C_{18});
b R=H, R′=COOR‴ (R‴=H, C_1-C_{18}), R″=COOR‴ (R‴=H, Me);
c R=Me, R′=Et, R″=COOH

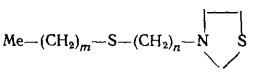
Yakovlev et al.[53] have shown that 2-glycosyl derivatives of thiazolidine protect yeast cells and *Escherichia coli* from the action of ionising radiation. Thiazolidine-2-carboxylic and -2,4-dicarboxylic acids and esters (LXXIXa, b), obtained by condensing glyoxylic acid and its esters with 2-aminoethanethiol and cysteine respectively[54,55], showed slight protective activity, as did compounds containing acetic-ester residues at position 2 (LXXVIId, e).[56] Among 2,2-dialkylthiazolidine-4-carboxylic acids a protective effect was observed only in (LXXIXc)[57]; 5,5-dimethylthiazolidine-4-carboxylic acid—a cyclic analogue of penicillamine—was inactive[51].



(LXXX)

a R=—$(CH_2)_6$—, b R=—O$(CH_2)_5$—, c R=MeO—$(CH_2)_4$—

The most important and interesting results were obtained in a study of the protective properties of *N*-substituted thiazolidines (LXXX). Westland et al.[16] investigated the action against radiation of fifteen 3-cycloalkylalkyl- and 3-aryloxyalkyl-thiazolidines. Several of them showed moderate activity, e.g. 3-6′-cyclohexylhexyl- and 3-5′-*o*-tolyloxypentyl-thiazolidines (LXXXa, b), whose protective indices were respectively 6.0 and 8.0. As among the amino-thiol derivatives containing an *N*-*p*-methoxyphenylalkyl substituent[17], only 3-4′-*p*-methoxyphenylbutylthiazolidine (LXXXc) showed sufficiently high protection, with I_{ip} = 7. Compounds with a branched polymethylene chain or with a 2-methyl group in the thiazolidine ring were devoid of activity. The thiazolidine derivative (LXXXc) gave weak protection when administered through the mouth.

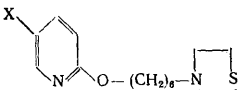


(LXXXI)

m=0—8, *n*=2—7

a *m*=5, *n*=6; b *m*=3, *n*=7; c *m*=4, *n*=5; d *m*=5, *n*=5

Most of the 3-alkylthioalkylthiazolidines (LXXXI) studied (> 25) afforded weak or no protection to irradiated mice on intraperitoneal administration, and only two compounds (a and b) had a moderately protective effect[58]. Oral introduction gave similar results, but (LXXXIa) protected weakly, then (LXXXIb). Furthermore, compounds (LXXXIc, d), relatively inactive on intraperitoneal administration, proved to be efficient when given orally: thus an oral dose of (LXXXIc) of 125 mg kg^{-1}, with LD_{50} = 650 mg kg^{-1}, protected 92% of mice, and its protective index was I_{or} = 10.



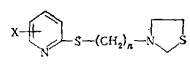
(LXXXII)

a X=5-Cl, b X=5-I

In contrast to pyrid-2″- and quinol-2″-yloxyalkylaminoethyl thiosulphates, among which protective agents of high efficiency on intraperitoneal introduction were discovered, their thiazolidine analogues (> 50 studied) were almost inactive with this method of administration[8]. However, two of them—3-6″-5‴-chloro- and 3-6″-5‴-iodo-pyrid-2‴-yloxyhexylthiazolidines (LXXXIIa, b)—were quite effective on oral administration, with protective indices respectively of ~ 7.0 and 6.0.

Compounds providing efficient protection on oral introduction were discovered also among 3-halogenopyrid-2'''-ylthioalkylthiazolidines (LXXXIII)[56] containing 3–10 methylene groups. The most active of them afforded no protection on intraperitoneal introduction (Table 7).

Table 7. Protective properties of the derivatives.



(LXXXIII)

X	n	Intraperitoneal administration				Oral administration			
		doses, mg kg^{-1}		survival, %	I_{or}	doses, mg kg^{-1}		survival, %	I_{or}
		LD_{50}	ED			LD_{50}	ED		
5-Br	5	275	100	93	5.3	800	200	73	6.9
5-Cl	7	56	30	20	0	650	75	60	14.0
5-Cl	8	125	70	8	0	500	125	80	7.2
3,5-Cl_2	7	275	125	60	3.5	1000	800	0	0

Thus quite efficient protective agents, which develop their activity predominantly on oral introduction, have been discovered among the > 140 thiazolidine derivatives studied, primarily among those substituted on the nitrogen atom. These results may provide some support for the hypothesis that thiazolidine compounds may act as long lasting forms of the corresponding 2-aminoethanethiol derivatives. However, it is still difficult, on the basis of existing data, to reach conclusions on the general effects of substituents in the thiazolidine ring on the protective action of these compounds and on differences in activity between intraperitoneal and oral administration.

6. 2-Aminoethanethiol Derivatives modified in the Hydrocarbon Chain

The structure of 2-aminoethanethiol—the primogenitor of protective agents—can be varied, not only by substitution at the amino and thiol groups, but also by modification of the hydrocarbon chain. Early studies had been made[3,59] of the effect of chain lengthening and branching on the protective activity. These investigations have recently been continued, and novel, more radical changes have been made in this part of the molecule.

$H_2N-(CH_2)_n-SX$ a X=H, n=2,6; b X=SO_3H, n=3,6–10;
(LXXXIV) c X=PO_3H_2, n=3

$H_2N-(CH_2)_m-NH-(CH_2)_n-SPO_3H_2$
(LXXXV)

A decrease in the protective effect until it completely disappears is confirmed on passing from the two-unit (ethylenic) chain in 2-aminoethanethiol to chains of three to six units (LXXXIVa)[60]. A similar rule is observed for the aminoalkyl thiosulphates (LXXXIVb)[15,30]. A sharp drop in protective activity is found also in the trimethylene analogue of Cystaphos (LXXXIVc)[34].

A rather different rule is found in *N*-aminoalkylaminoalkyl phosphorothiolates (LXXXV)[34]. Depending on the length m of the polymethylene chain in the substituent, increase in the distance between the sulphur and nitrogen atoms from two to three methylene units may either enhance or diminish the protective efficiency (Table 8).

The compound (LXXXV: $n = m = 3$) is one of the most efficient protective agents among derivatives of aminoalkyl phosphorothiolates.

Gandacek and Swartz[61] tried to discover a connection between the protective activity of amino-thiols and the possibility of intramolecular hydrogen bonding between the nitrogen and sulphur atoms. They showed that such a bond can be formed only in the first member of the series, 2-aminoethanethiol, which in the crystalline state has the gauche conformation. In their view, however, it is improbable that this fact will be significant in the establishment of a protective effect, since the conformation will certainly change under physiological conditions—in solution.

$H_2N-CHCH_2S-X$ (LXXXVI)
Me

H_2N-CH_2CHS-X (LXXXVII)
Me

a X=SO_3H, b X=H

Table 8. Protective properties of derivatives (LXXXV).

LXXXV, m	n = 2				n = 3			
	doses, mg kg^{-1}		survival, %	I_{ip}	doses, mg kg^{-1}		survival, %	I_{ip}
	LD_{50}	ED			LD_{50}	ED		
2	1300	400	100	6.5	1300	500	100	5.2
3	700	300	86	4.3	560	75	80	13.5
4	800	200	80	7.2	225	100	13	0

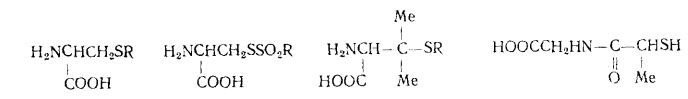
Investigations have continued during recent years on the effect of branching in the ethylene chain in compounds having the 2-aminoethanethiol structure on their toxicity and protective activity. Attachment of a methyl group to the carbon atom adjacent to the nitrogen atom in *S*-aminoethyl thiosulphate (LXXXVIa) maintains both activity and toxicity, whereas the isomer having the methyl group attached to the carbon adjacent to the sulphur atom (LXXXVIIa) is considerably less toxic, but completely devoid of protective action. It is interesting that the opposite relation is observed with the two analogous amino-thiols (LXXXVIb) and (LXXXVIIb)[30]. The trimethylene analogue of aminoethylthiouronium and certain derivatives substituted on the second carbon atom were less active than itself[62].

$H_2NCH_2CHCH_2-S-C(=\overset{+}{N}H_2)-NH_2$
R
(LXXXVIII)
R=H, OH, Cl, Br

$H_2N-(CH_2)_3-NH-CRR'-CH_2S-X$
(LXXXIX)
X=H, SO_3H, PO_3H_2

Detailed study of the effect of methylating the carbon atom adjacent to the nitrogen atom in the compounds (LXXXIX) on their protective activity and toxicity revealed no general rule[34]. Introducing a single methyl group into these compounds with X = H, SO_3H hardly affects the toxicity or activity, whereas when X = PO_3H_2 it increases the toxicity and decreases the activity. Replacing a second hydrogen atom by methyl leads to a sharp increase in toxicity and loss of activity when X = H; with X = SO_3H, PO_3H_2, however, the toxicity diminishes, while the

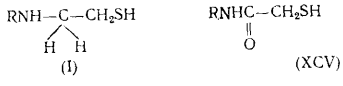
Bunte salt remains inactive, whereas the phosphorothiolate becomes even more effective than the first member of the series (R = R′ = H).



(XC, R=H) (XCI, R=SO_3H) (XCII) R=Me, *p*-MeC_6H_4 (XCIII) a R=$MeSO_2$ (XCIV) (Thiola)

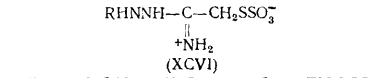
The search for protective agents has continued among derivatives of cysteine (XC), which was the first to protect animals from ionising radiation[3]. Japanese workers[63] made a detailed study of the antiradiation action of the ethyl ester, administered both intraperitoneally and orally. This relatively non-toxic compound was similar to cysteine in protective action, but did not protect mice from an absolutely lethal dose of radiation. The Bunte salt (XCI) was less active than cysteine itself[30]. Among the more complicated derivatives (XCII)[64] and (XCIII)[65], moderate protective activity was shown only by (XCIIIa).

Interesting results have been obtained during recent years from more fundamental changes in the hydrocarbon chain of amino-thiols. Sugahara et al.[66,67] discovered that α′-mercaptopropionylglycine (XCIV), which they termed "Thiola", while being relatively non-toxic (intraperitoneal LD_{50} = 2000 mg kg^{-1}), has an effect against radiation when small doses (20–40 mg kg^{-1}) are given in experiments on mice. However, it protects animals only at radiation doses leading to destruction of at most 70% in a control group. According to these workers[67] Thiola exerts a curative effect, both with parenteral and with oral application, on humans subjected X-radiotherapy: chromosome breakages in leucocytes become fewer after administration of this preparation. A Swedish patent[68] described the production not only of Thiola but also of several other derivatives of this type.



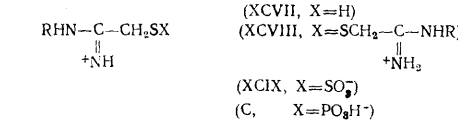
(I) (XCV)

The above work continued earlier investigations of the protective action of mercaptoacetamides (XCV)[69,70], which can be regarded as derived from 2-aminoethanethiol (I) in which the methylene adjacent to the nitrogen atom has been replaced by a carbonyl group. In 1969 Fridinger and Robertson[71] published a study of the protective action of four substituted acetamidrazone thiosulphates (XCVI). They provided weak protection from radiation for mice. It is readily seen that these compounds can be regarded as having the same type of modification of the ethylene chain: two hydrogen atoms have now been replaced not by carbonyl but by the isosteric imino-group.



(XCVI)
R=*p*-$NO_2C_6H_4$, *o*-MeC_6H_4, *p*-FC_6H_4, $EtOOCCH_2$

This latter work was probably the origin of studies by American workers headed by Westland[72] on the protective activity of 84 derivatives of mercaptoacetamidine (XCVII) and its *S*-functional substitution products—disulphides (XCVIII), thiosulphates (XCIX), and phosphorothiolates (C)—with various substituents attached to the nitrogen atom.



(XCVII, X=H) (XCVIII, X=SCH_2—C(=$^+NH_2$)—NHR) (XCIX, X=SO_3^-) (C, X=PO_3H^-)

The simplest compounds of this type—mercaptoacetamidines (XCVII)—far exceeding the corresponding aminoethanethiols in toxicity, were quite effective both with intraperitoneal and with oral administration. The most active among them was the compound with a free amino-group (XCVIIa: X = H), as well as the adamant-1-ylmethyl and 3,5-dimethyladamant-1-ylmethyl derivatives (XCVIIb, c). It is interesting that they were more effective when administered orally (Table 9). The distance of the bulky adamantyl group from the amidine nitrogen atom had little effect on the activity.

The oxidised forms of the mercaptoacetamidines—the corresponding disulphides (XCVIII)—are somewhat inferior in efficiency on intraperitoneal administration, but rather better when introduced orally. Data on the most efficient compounds of this series—the *N*-unsubstituted disulphide (XCVIIIa), adamant-1-ylmethyl, 3,5-dimethyladamant-1-ylmethyl, and cycloheptylmethyl derivatives (XCVIIIb-d)—are included in Table 9. It is noteworthy that the adamantyl derivatives are inactive on intraperitoneal administration. The compound (XCVIIIb) is the most effective of all known oral protective agents studied on mice: its therapeutic index is ~ 13, and its protective index ~ 20.

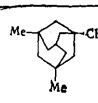
The largest group among the compounds studied (56) comprised the Bunte salts (XCIX) with cycloalkyl-, aryl-, heteryl-, and hydroxy-alkyl substituents attached to the nitrogen atom. Most of them were considerably more toxic than the corresponding aminoethyl thiosulphates, and had a medium and low protective effect. Only three compounds—the 3′,4′-dimethoxyphenylethyl, indol-3′-ylethyl-, and *cis*-2-myrtanyl-acetamidine thiosulphates (XCIXe-g)—showed high efficiency as intraperitoneal protective agents (Table 9). It is interesting that the immediate homologue of (XCIXf), with three methylene groups between the indole ring and the nitrogen atom, is completely inactive. The vast majority of Bunte salts studied did not protect mice from radiation when given orally, and only one compound—the *N*-born-2-yl derivative (XCIXh)—showed a fairly high protective effect with this mode of introduction.

The paper[72] gives results for only four guanylmethyl phosphorothiolates (C). Three of them—the unsubstituted compound (Ca), cycloheptylmethyl (Cd), and cyclooctylmethyl derivatives—exhibit slight protective activity with both methods of administration. Unique behaviour was exhibited by *S*-N^1-3′,5′-dimethyladamant-1′-ylmethylguanylmethyl dihydrogen phosphorothiolate (Cc), which under the experimental conditions was considerably more efficient than all known protective agents on intraperitoneal introduction (Table 9): its therapeutic index exceeded 30, and its protective index was $I_{ip} \simeq 50$. Its protective effect was not so high when used orally.

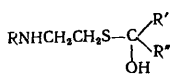
Comparison of the most efficient protective agents of acetamidine structure indicates that activity is increased by the introduction of the bulky adamantyl group attached to the nitrogen atom by a single methylene unit. However, no general rules could be derived for the influence of substituents in the amidino-group or of various functional

Table 9. Protective properties of the derivatives

$RHN-C(=H_2N^+)-CH_2SX$

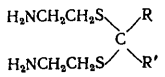
R	X	Compound	Intraperitoneal				Oral			
			doses, mg kg^{-1}		survival, %	I_{ip}	doses, mg kg^{-1}		survival, %	I_{or}
			LD_{50}	ED			LD_{50}	ED		
H	H	XCVII a	52	12	73	7.5	150	20	67	12.5
	disulphide	XCVIII a	60	12.5	100	9.6	125	25	67	8.9
	SO_3^-	XCIX a	87	50	100	3.5	300	100	73	5.2
	PO_3H^-	C a	100	37.5	93	6.0	135	37.5	73	6.2
	H	XCVII b	22	6	67	6.0	65	15	93	8.6
	disulphide	XCVIII b	100	50	7	0	325	25	53	20.0
	SO_3^-	XCIX b	25	10	93	4.8	300	200	0	0
	H	XCVII c	10	5	64	3.3	175	25	80	12.5
	disulphide	XCVIII c	5	3	40	0	250	25	53	15.3
	SO_3^-	XCIX c	44	15	27		600	600	7	0
	PO_3H^-	C c	125	8	93	0				
				4	60	50	425	100	100	15
	disulphide	XCVIII d	22	5	70	7.5	188	25	73	13.0
	PO_3H	C d	38	20	70	2.9	40	20	60	3.2
3,4-$(MeO)_2C_6H_3(CH_2)_2$	SO_3^-	XCIX e	250	50	60	8.0	900	600	0	0
Indol-3'-ylethyl	SO_3^-	XCIX f	180	14	67	21.5	600	500	0	0
cis-Myrtan-2-yl	SO_3^-	XCIX g	63	8	67	13.0	380	200	20	0
Born-2'-yl	SO_3^-	XCIX h	30	15	93	3.9	225	50	87	8.4

derivatives involving substitution at the sulphur atom. The data cited here demonstrate that the most efficient protective agents in experiments with both intraperitoneal and oral introduction into mice occur among compounds of mercaptoacetamidine structure.



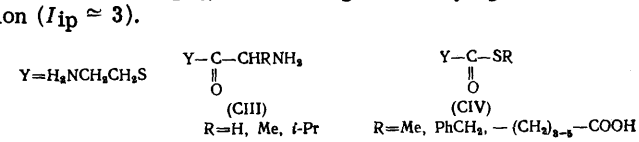
(CI)

R=H, Ac; R'=H, CF_3; R"=CCl_3, CBr_3, CF_3
a R=R'=H, R"=CCl_3; b R=R'=H, R"=COOR"' (R"'=C_1–C_{18}); c R=R'=H, R"=COOMe



(CII)

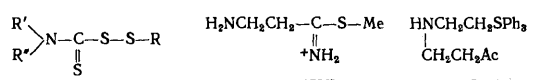
A few other groups of 2-aminoethanethiol derivatives, differing significantly in structure from the above, have been studied as protective agents. This applies primarily to products formed by reaction with carbonyl compounds. Field et al.[73] studied a series of monothiohemiacetals (CI), and found that one of them (CIa) developed a strong protective action, but in doses close to toxic. French workers[54,55] discovered an extremely efficient protective agent—the hydrochloride of methyl *S*-2'-aminoethylthioglycollate (CIc)—among a large number of condensation products (CIb) of aminoethanethiol with glyoxylic esters. In its prophylactic protective effect in an intraperitoneal dose of 450 mg kg^{-1} ($\frac{1}{2}LD_{50}$) it surpasses 2-aminoethanethiol and aminoethylthiouronium, while being considerably less toxic. Among mercaptals (CII)[51] a single compound (R = R' = $COOC_2H_5$) showed slight activity against radiation ($I_{ip} \simeq 3$).



(CIII) R=H, Me, *i*-Pr

(CIV) R=Me, $PhCH_2$, $-(CH_2)_{3-5}-COOH$

Rachinskii et al.[74] prepared and studied the protective action of several aminoethanethiol derivatives (CIII) *S*-acylated by amino-acids—glycine, alanine, leucine, etc.—which were less toxic than aminoethanethiol but exhibited the same protective effect in considerably larger doses. The dithiocarbonates (CIV) were relatively ineffective[75], and trithiocarbonates (CV) showed no activity[76].

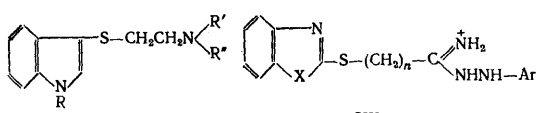


(CV) R=CH_2CH_2NHAc; R'=R"=H, Me

(CVI)

(CVII)

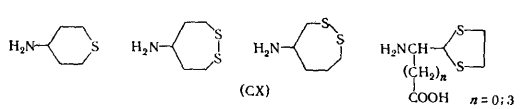
A slight protective effect was shown by the thioimidic ester (CVI)[77] and by the *S*-triphenylmethyl derivative (CVII)[23], for the latter of which a prolonged protective action was assumed. A few *S*-indol-3'-yl derivatives of the type (CVIII) have been synthesised in which R = R' = R'' = H or CH_3, but no results are reported for the protective activity[78].



(CVIII)

(CIX) X=S, NH; *n*=1, 2

Interesting investigations were made by Pantev et al.[79,80] in a search for protective agents among *S*-benzazol-2'-ylthioalkanoamidrazones (CIX). The most active was the benzimidazole derivative (CIX: X = NH, *n* = 2, Ar = *p*-$CH_3C_6H_4$): a dose of 120 mg kg^{-1} protected 56% of mice.



(CX)

a b c d

Several cyclic analogues of amino-thiols with one or two sulphur atoms in the ring (CXa–d) were studied[18,81,82], and all proved to be inactive.

Thus the most efficient protective agents for intraperitoneal and/or oral use under experimental conditions have been found among the almost 150 compounds of amino-thiol structure and having a modified hydrocarbon chain that have been studied.

The information surveyed above shows that more than 900 compounds of amino-thiol structure have been studied during recent years, and among them several highly efficient protective agents under experimental conditions have been discovered. A characteristic feature of the chemical structure of most of them is the presence of a cycloalkyl, adamantyl, aryl, or pyridyl substituent attached to the nitrogen atom through an alkyl, oxyalkyl, or thioalkyl chain.

No data or hypotheses have been published on the role of these structural factors in the development of protection from radiation. The presence of a sufficiently heavy, bulky substituent, usually containing 9–13 carbon atoms, may be supposed to strengthen intermolecular interactions and steric effects and to change the conditions of fixation of such compounds in cells and tissues of the living organism, which will undoubtedly influence the permeability to, the transport, and the distribution of these substances. All this evidently leads in aggregate to an increase in the biological activity of such compounds, when the decrease in the effective protective dose is usually greater than that in the toxic dose (e.g. LD_{50}), which increases the interval between them, i.e. the therapeutic latitude of these substances.

With regard to the thiol function in protective agents of this type, the phosphorothiolate and the disulphide groups must be regarded as optimal for intraperitoneal introduction, and the disulphide and thiazolidine groups for oral administration.

An extremely promising line of research has been fundamental modification of the hydrocarbon chain. The most efficient protective agents have been found among compounds of this type—*S*-N^1-3′,5′-dimethyladamant-1′-ylmethylguanylmethyl dihydrogen phosphorothiolate (Cc) on intraperitoneal administration and bis-N^1-adamant-1′-ylmethylguanylmethyl disulphide (XCVIIIb) when given orally.

X—CH_2CH_2SH (CXI)

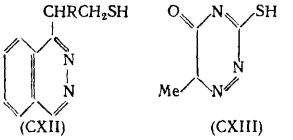
a—X=NH_2, b X=—C(=$\overset{+}{N}H_2$)—NH, c X=—NH—C(=$\overset{+}{N}H_2$)—NH_2, d X=SO_3H, e X=SO_2Et

All the results that have accumulated during recent years compel us to change our existing view[3] that the presence of a free amino-group is a necessary condition for the development of high protective activity in compounds having an amino-thiol structure. Kostyukovskii et al.[83] have recently shown that the amino-group in 2-aminoethanethiol (CXIa) can be replaced by several other electron-accepting groups—e.g. amidino, guanidino, sulpho, and sulphonyl (CXIb–e)—without a significant decrease in protective activity. These authors concluded that the protective activity of compounds of type (CXI) is due to the reactivity of the mercapto-group, which can be represented quantitatively by the dissociation constant K_a^{SH}: effective compounds with this structure should have pK_a^{SH} = 7.7–8.7 (the value of this exponent for 2-aminoethanethiol is 8.2).

The information in the following Section may serve to confirm that the presence of an amino-group or other nitrogen-containing function is not necessary for the development of a high protective effect, not only in the aminoethanethiol type of compound but also in sulphur-containing compounds in general.

III. OTHER SULPHUR-CONTAINING COMPOUNDS

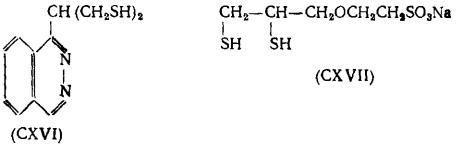
Protective agents have been found during recent years among sulphur-containing compounds of non-aminothiol structure—thiols, thiosulphates, sulphides, di- and trisulphides, dithiocarboxylic acid derivatives, sulphoxides, sulphones, etc.



(CXII) (CXIII) (CXIV) (CXV)

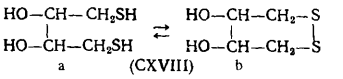
a R=CN, b R=Ph, c R=COOEt

Mercaptoalkyl derivatives of phthalazine (CXII) exhibit slight protective activity[84]. The 5,6-dihydro-3-mercapto-5-oxotriazine (CXIII) is moderately protective[85].



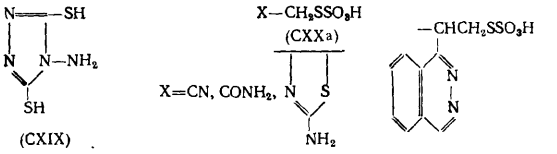
(CXVI) (CXVII)

Several studies have been made of the action of various dithiols against radiation. Foye showed[86] that, in contrast to the inactive dimercaptomethylenemalononitrile (CXIVa), the unsaturated mononitriles (CXIVb, c) develop appreciable protective activity. A slight increase in the survival rate of irradiated mice was produced by the prophylactic administration of racemic dimercaptosuccinic acid and its *meso*-form (CXV)[87]. A comparatively slight protective effect was observed with the dithiols (CXVI)[84] and (CXVII)[88].



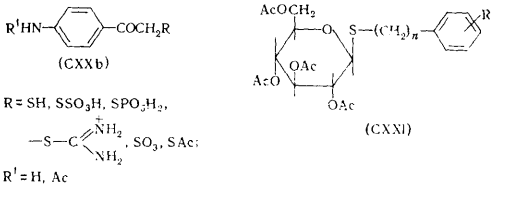
a (CXVIII) b

The attention of radiobiologists has been attracted during recent years to dithiothreitol (CXVIIIa)[89–92], which exists in the less toxic[90] cyclic form (CXVIIIb). It was relatively ineffective as a protective agent. Better results were obtained by its medicinal use under the experimental conditions. The *D*-isomer is more active than the *L*-form[91]. The di-*O*-acetyl derivative of (CXVIII) has a weak protective action[92].



(CXIX) (CXXa)

Some increase in the survival rate of irradiated mice was observed when the aminotriazoledithiol (CXIX) was used[93].

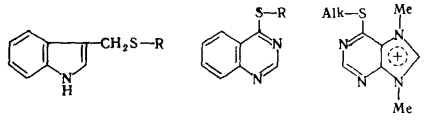


(CXXb) (CXXI)

R = SH, SSO_3H, SPO_3H_2, —S—C(=$\overset{+}{N}H_2$)—NH_2, SO_3, SAc;

R′ = H, Ac

No activity has been discovered among various types of compounds (CXXa) containing a thiosulphuric acid residue[30,79,84]. Kostyukovskii et al.[94] showed that, in a series of *p*-aminobenzoylmethanethiol derivatives (CXXb), a pronounced protective action was exerted by the phosphorothiolate and the compound containing an *S*-acetyl group.

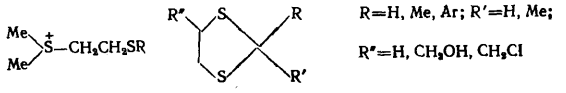


(CXXII) (CXXIII) (CXXIV)

Several compounds of sulphide structure have been studied. Ishiguro et al.[95] found moderate protective action in certain thioglycosides of type (CXXI), of which the most active had R = H and $n = 1, 2$. In the search for protective agents several sulphides were synthesised with heterocyclic and aryl groups of the types (CXXII)–(CXXIV)[96–98].

(CXXV) (CXXVI)

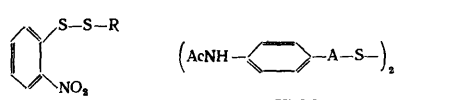
Thien-2-ylmethanol (CXXV), a cyclic analogue of mercaptoethanol, can be included formally among sulphides. A freshly prepared specimen has a weak protective action[99], but after standing for 1 month or exposure to a 1000-W lamp for 18 h this substance shows a fairly strong protective effect. It was assumed[99] that polymerisation occurred under these conditions. Bitoun et al.[100] prepared 13 cyclic analogues of mercaptoethanol of a different type: among these oxathiolans (CXXVI) only the 2,2-dimethyl, 5-chloro-2,2-dimethyl, and spirocyclohexane derivatives exhibited a protective effect of 20–50% on mice.



(CXXVII) (CXXVIII)

R=H, Ac

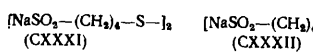
Prophylactic introduction of ethane-1,2-dithiol derivatives (CXXVII) produced a slight increase in survival rate of irradiated mice[14]. A detailed investigation of the protective properties of > 30 dithiolans (CXXVIII)—cyclic analogues of ethane-1,2-dithiol—has shown[101] that they include compounds that ensure 50–80% survival of mice after intraperitoneal doses close to $\frac{1}{2}LD_{50}$, when animals in a control group are completely destroyed. These are aryl derivatives (R′ = R″ = H; R = Ar) containing a phenyl, a *p*-chloro-, *p*-hydroxy-, or *p*-methoxy-phenyl, or a *p*-tolyl substituent at the 2 position in the ring.



(CXXIX) (CXXX)

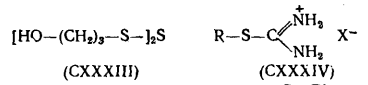
A=CH_2CH_2, CH_2CO, COCH(Me)

Several disulphides and their derivatives have been prepared, and their protective activity has been studied. The absence of biological data prevents assessment of the prospects for unsymmetrical aryl disulphides (CXXIX)[102], disulphides of type (CXXX)[103], or disulphides of the pyrimidine series[104] as protective agents.



(CXXXI) (CXXXII)

High protective activity in experiments on mice was shown by the symmetrical disulphide (CXXXI), which is a derivative of butanesulphinic acid[29]. An intraperitoneal dose of 200 mg kg^{-1} (LD_{50} = 800 mg kg^{-1}) protects 73% of mice that have been irradiated with the absolutely lethal dosage ($I_{ip} \simeq 7$). The corresponding trisulphide (CXXXII) was a still more efficient protective agent[29]. While possessing low toxicity (both intraperitoneal and oral LD_{50} = 900 mg kg^{-1}), this compound at an intraperitoneal dose of 38 mg kg^{-1} is claimed to protect 78% of mice when a control group undergoes absolute destruction ($I_{ip} > 41$), and an oral dose of 300 mg kg^{-1} ensures complete survival of the animals ($I_{or} \simeq 6$). Bis-3-hydroxypropyl trisulphide (CXXXIII) has shown[105] a slight protective effect in experiments on mice.



(CXXXIII) (CXXXIV)

a—R=Et

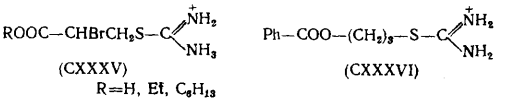
Several papers have appeared on the search for protective agents among alkylthiouronium derivatives, analogues of ethylthiouronium (Etiron, CXXXIV), which exerts a quite pronounced effect. According to Zherebchenko and his coworkers[106] the size of the alkyl group in compounds of this type has a significant influence on the protective activity (Table 10), whereas the nature of the anion plays no special part. It was suggested that Etiron differs from amino-thiols in the mechanism of its protective action. Mukhin et al.[107] supposed that tissue hypoxia underlay the mechanism of protection by Etiron. They report that, in experiments both on mice and on rats, this compound considerably surpasses *S*-2′-aminoethylthiouronium in efficiency.

Table 10. Effect of size of alkyl group in compounds (CXXXIV) on their protective properties[106].

CXXXIV R	Survival of mice, %
Me	40.0
Et	49.0
n-Pr	37.6
n-C_9H_{19}	2.8
Control	1.8

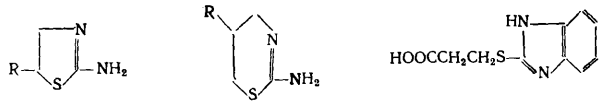
In order to examine the effect of the structure of the *S*-alkyl substituent and of the anion Mizrakh et al.[108] studied several phosphorus-containing alkylthiouronium derivatives both at a cellular level and in experiments on mice with prolonged irradiation (dosage rate 5.8 rad min^{-1}). All the compounds were significantly superior in protective activity to Etiron, which hardly protected the animals at all under these conditions; it was thought that this might be due to the duration of irradiation. The most active compounds were *S*-n-butylthiouronium n-butyl

hydrogen phosphite (CXXXIV: R = C_4H_9 and X = $C_4H_9OPHO_2$) and *S*-ethylthiouronium diethyl orthophosphate (CXXXIV: R = C_2H_5 and X = $(C_2H_5O)_2PO_2$), which ensured the protection of 70–80% of mice and acted against radiation at the chromosomal and cellular level[108].



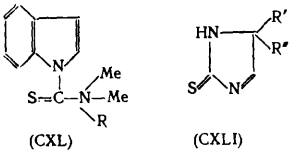
(CXXXV) R=H, Et, C_6H_{13} (CXXXVI)

Slight activity was shown by thiouronium derivatives of α-bromopropionic acid and its esters (CXXXV)[82,109] and also by 3′-benzoyloxypropylthiouronium (CXXXVI)[109]. 2-Acyloxypropyl and other derivatives of thiouronium were inactive.



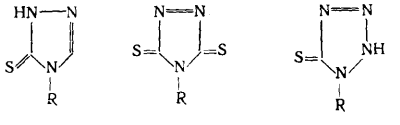
(CXXXVII) R=H, Me, CH_2OH, Br (CXXXVIII) R=H, Cl, Br (CXXXIX)

The protective action of several cyclic analogues of thiouronium of the types (CXXXVII) and (CXXXVIII)[82,110] and (CXXXIX)[79] has been studied. The most interesting results were obtained with 2-aminothiazoline (CXXXVII: R = H)[110]—a possible conversion product of aminothiouronium in the organism—and also for certain of its 5-substituted derivatives, which approach aminoethylthiouronium in efficiency on prophylactic intraperitoneal administration.



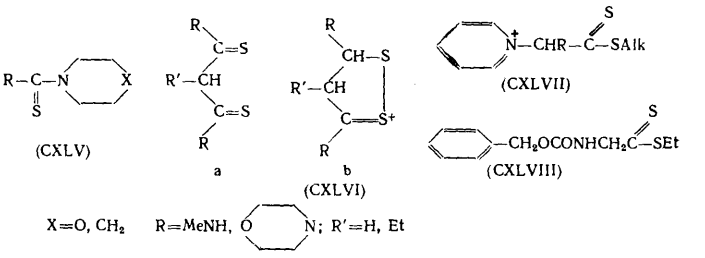
(CXL) (CXLI)

Thiourea derivatives containing a quaternary nitrogen atom (CXL), which are similar in structure to thiouronium compounds, were prepared by Tulecki et al.[111] to study their action against radiation. Here we can also mention cyclic analogues of thiourea—derivatives of imidazole (CXLI)[49,112], triazole (CXLII) and (CXLIII), and tetrazole (CXLIV)[113]—which are able to exist in the tautomeric thiol form. The most efficient were the *p*-halogenoaryltetrazolethiones (CXLIV: R = *p*-HalC_6H_4).



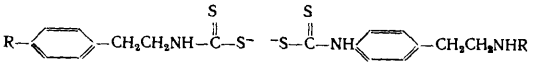
(CXLII) (CXLIII) R=Ar (CXLIV)

Several other compounds containing a thiocarbonyl group were studied in the search for protective agents. Bitoun et al.[114] studied the action against radiation of several morpholino- and piperidino-thioamides (CXLV), and found that only a few of them had a slight protective effect. Similar results were obtained for a series of dithioamides (CXLVIa). Cyclic analogues of the latter—1,2-dithiolium derivatives (CXLVIb)—only slightly surpass in activity (survival of mice at most 30–40%) the initial thioamides[115].



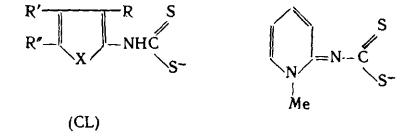
(CXLV) a b (CXLVI) X=O, CH_2 R=MeNH, O N; R′=H, Et (CXLVII) (CXLVIII)

Great attention has been paid during recent years to the search for protective agents among dithiocarboxylic acid derivatives. This line of attack was developed especially intensely by Foye and his coworkers, who showed that substituted derivatives of pyridinodithioacetic acid (CXLVII)[116] and the analogue (CXLVIII)[93] were moderately active in experiments on mice.

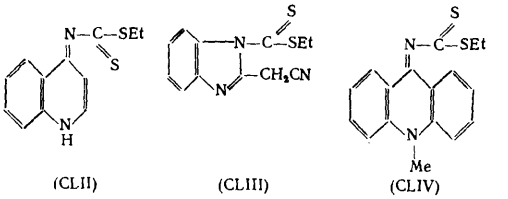


a (CXLIX) b

Several dithiocarbamates have been prepared and studied. No protective activity was detected in two types of derivatives of dithiocarbamic acid based on phenylethylamine (CXLIXa, b)[117], as well as in furan and thiophen derivatives (CL)[118]. It was shown for 1′-methylpyrid-2′-yldithiocarbamic acid (CLI)[119] that dithiocarbamates of the stronger bases have a more pronounced protective effect, though the percentage survival of mice when this compound is used as the 2-amino-1-methylpyridinium salt is not high. Dithiocarbamates of the corresponding 4-imino- and 2-imino-1-methyl-pyrimidines exhibit no protective activity. Among dithiocarbamic esters of 4-amino-2-methylquinoline (CLII), benzimidazole (CLIII), and 9-amino-10-methylacridine (CLIV) only the last showed action against radiation[120].

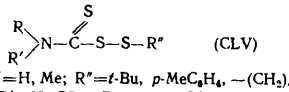


(CL) X=O,S; R=CN, COOEt; R′=H, Me, Ph (CLI)



(CLII) (CLIII) (CLIV)

Field and his coworkers found[76,121] that some of the trithiocarbamates studied by them (CLVa, b) possess quite pronounced protective activity when introduced in large doses.



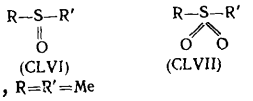
(CLV)

R=R′=H, Me; R″=*t*-Bu, *p*-MeC_6H_4, $-(CH_2)_4SO_2Na$

a R=R′=H, R″=*t*-Bu; b R=R′=Me, R″=*t*-Bu

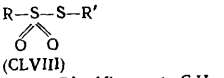
Tulecki et al.[111,122] synthesised several heterocyclic arenesulphinamide derivatives, but gave no data on their protective action.

Studies have continued on the protective action of diammonium phosphoramidothioate[123-125] and its analogues[123], which exhibited little or no activity.



(CLVI) a, R=R′=Me (CLVII)

Compounds containing quadrivalent and sexivalent sulphur have also been studied—as well as bivalent compounds—for use as protective agents. It had earlier been shown[3] that dimethyl sulphoxide (CLVIa) has a protective action against the general irradiation of mice. Arzamastsev et al.[126] studied 40 analogues of this compound (CLVI) and of sulphones (CXVII) with alkyl, ethylenic, vinyl, and acetylenic groups. Only three of these compounds—(CLVI: R = CH_2:CH and R′ = CH_2:CH.SO.$[CH_2]_2$), (CLVI: R = R′ = t-C_4H_9), and (CLVII: R = CH_3 and R′ = CH_2:CH)—had a moderate action against radiation in doses of 33–50% of LD_{50}. Certain thiosulphones (CLVIII) were inactive[64].



(CLVIII) R=Me, p-MeC_6H_4; R′=Alk, cyclo-C_6H_{11}

A comparative study has been made during recent years of the protective action of the selenium analogues of certain sulphur-containing agents[127-129]. Selenourea protects mice more effectively than does thiourea. The protective action of the selenium analogue of cysteine and certain other selenium compounds is at the same level or even higher, but they are considerably more toxic than the corresponding sulphur compounds.

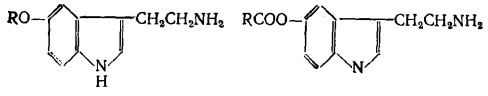
Thus a few highly efficient protective agents, developing activity on intraperitoneal and oral administration in an experiment, have also been discovered among the many (~ 300) sulphur-containing compounds of non-aminothiol structure studied as protective agents against radiation.

IV. HETEROCYCLIC COMPOUNDS

The search for protective agents has been made among nitrogen-containing heterocycles during the past five or six years, as in previous years. Among them derivatives of indole have attracted the greatest attention.

Indolylalkylamines

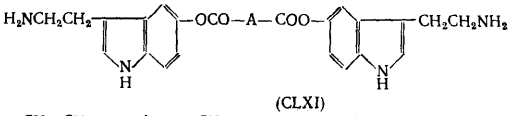
Comprehensive investigations on methods for the synthesis of indolylalkylamines and on their antiradiation properties, made in our country during recent years by Suvorov, Zherebchenko, Semenov, Ermonenko, Shashkov, Antipov, and others[130], led to the production of the protective preparation Mexamine (CLIXa), a close analogue of serotonin (CLIXb), and formed the basis for a further successful search for protective agents in this series of compounds. The study was continued of *N*-peptide derivatives of indolylalkylamines, which showed a marked protective effect (survival of mice 40–60%).[130]



(CLIX) (CLX)

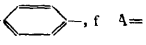
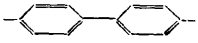
a R=Me (Mexamine)
b R=H (Serotonin)
c R=Et

Investigation of the protective properties of a large number of *O*-acyl derivatives of serotonin (CLX)[130-133]—acyl analogues of Mexamine—showed that the introduction of residues of saturated aliphatic acids at the phenolic hydroxyl does not diminish the protective action in comparison with serotonin or Mexamine. Lengthening of the carbon chain in the acyl substituent is accompanied by enhancement of toxicity. Both in the pronounced character of their protective effect and in its duration these compounds are hardly distinguishable from serotonin. Also, like serotonin, they possess little antiradiation activity when taken. *O*-Aroyl and urethane derivatives (CLX: R = CH_3NH, p-ClC_6H_4NH) have a weaker protective effect.



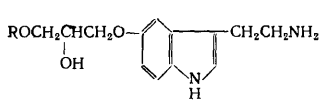
(CLXI)

a A = —CH=CH—, b A = $-(CH_2)_2-$, c A = $-(CH_2)_4-$, d A = $-(CH_2)_8-$

e A =  , f A = 

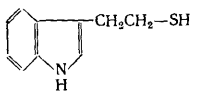
Several other derivatives of serotonin have been prepared and studied in order to find among indolylalkylamines protective agents of prolonged action and active on oral administration. Interesting results have been obtained for diesters (CLXI) formed by dicarboxylic acids—fumaric, adipic, sebacic, terephthalic, and biphenyl-*pp*′-dicarboxylic—with serotonin[132]. These compounds also are the equal of serotonin and Mexamine in protective activity. Their toxicity is on the average several times higher than that of the latter. When introduced into mice at different times before irradiation, they exhibited more prolonged action against radiation than did serotonin or Mexamine. Data for several of these compounds show (Table 11) that the most efficient as a protective agent is that derived from succinic acid (CLXIb), with $I_{ip} = 20$. Compounds (CLXId, e) retain their high protective properties for 1 h, in contrast to Mexamine and serotonin. When taken orally the bis-*O*-acyl derivatives, like the monoacyl compounds, exert a slight protective effect.

Addition of a glycerol molecule to tryptamine at position 5 of the indole ring (CLXIIa)[132] enhances the effectiveness of tryptamine against radiation. Prophylactic application of this compound gives 60% survival of mice with 92% mortality of animals in a control group. Replacement of the γ-hydroxyl by an alkoxy-group (CLXIIb) does not enhance the antiradiation properties, and introduction of a hydroxyethyl group (CLXIII) leads to a loss of activity. The *O*-glucoside of serotonin and derivatives of 3-dialkylamino-3-deoxy-analogues of 1-indol-3′-ylglycerol were ineffective[133].

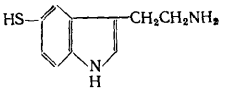


(CLXII) a R=H, b R=Alk
(CLXIII) R=HO—$(CH_2)_2$—

Comparing protective activities in experiments under the same conditions, Deanovič showed[134] that serotonin somewhat surpasses Mexamine, and 5-ethoxytryptamine (CLIXc) is inferior to both. He even[135] discovered that the thiol analogue of tryptophol (CLXIV) and the corresponding disulphide exerted no strong action against radiation, whereas 5-mercaptotryptamine (CLXV) protected mice only slightly more weakly than did serotonin, even with a superlethal dose of radiation.



(CLXIV)

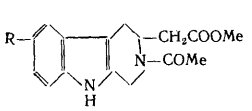


(CLXV)

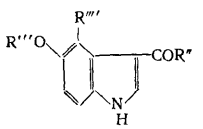
Table 11. Protective properties of serotonin, Mexamine, and their analogues (CLXI)[132].

CLXI A	Doses, mmole kg^{-1}		Time to irradiation, h	Survival, %	I_{ip}
	LD_{50}	ED			
a	0.288	0.070	0.1	60.0±10.9	6.6
			1.0	27.6±8.3	
			2.0	20.0±12.6	
b	0.800	0.070	0.1	75.0±9.7	20.0
			1.0	35.0±10.7	
			2.0	10.9±9.5	
c	0.324	0.070	0.1	60.0±10.9	8.5
			1.0	36.6±8.8	
			2.0	0	
d	0.107	0.070	0.1	67.8±8.9	2.6
			1.0	55.1±9.4	
			2.0	20.0±12.6	
e	0.084	0.070	0.1	94.7±9.15	2.3
			1.0	51.8±9.6	
			2.0	10.0±9.5	
Mexamine	1.04	0.30	0.1	53.8±9.8	18.6
		0.10	0.1	78.5±13.3	
		0.30	0.3	33.3±12.2	
		0.10	0.3	0	
Serotonin		0.04	0.1	64.0±11.3	
		0.150	0.3	0	
		0.40	0.3	6.7±6.5	

From tryptophol Japanese workers[136] prepared several compounds of tryptamine structure, including tricyclic compounds, e.g. (CLXVI), but they did not report results of their biological tests.



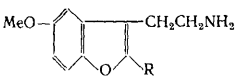
(CLXVI)



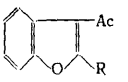
(CLXVII)

Among the many (~ 100) indole compounds studied of type (CLXVII), containing a 3-carbonyl group, Shadurskii and Maksimenko[137] were unable to find any which would protect irradiated mice by more than 20–30%. These workers and also Il'yuchenko et al.[138] studied the protective activity of several types of benzofuran compounds (CLXVIII–CLXX), which are isosteric with indole compounds and include an analogue (CLXVIII) of Mexamine.

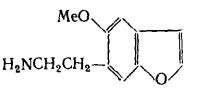
Most active among them (40% protection) was the aminoethyl derivative (CLXX)[138].



(CLXVIII)

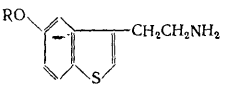


(CLXIX)

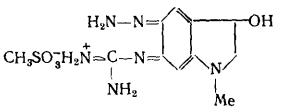


(CLXX)

According to Deanovič[135] the benzothiophen analogue (CLXXIa) of Mexamine has no action against radiation at all, whereas the isostere (CLXXIb) of serotonin is closely similar in efficiency to the latter, becoming inferior only at superlethal radiation doses[135,136].



(CLXXI a R=Me, b R=H)

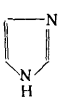


(CLXXII)

Japanese workers[139,140] made a detailed study of the protective properties of 5-hydrazonoadrenochrome-6-guanidinium methanesulphonate (CLXXII), which is a modification of an indoline metabolite. This relatively non-toxic compound (subcutaneous LD_{50} = 1834 mg kg^{-1}) shows a pronounced action against radiation in small doses of ~ 5 mg kg^{-1}. Under the name "S-adchnon" this protective agent, which acts on haemapoietic organs, has been proposed for clinical application to diminish the harmful effect of irradiation during the X-radiotherapy of human beings.

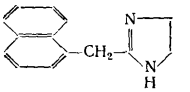
Other Nitrogen-containing Heterocycles

Investigation of the protective activity of imidazole (CLXXIII) and its derivatives has continued during recent years[141–143]. An intraperitoneal dose of imidazole itself of 350 mg kg^{-1} introduced 5 min before irradiation protects ~ 80% of mice; introduction 4½ h before and 1 min after irradiation halves the protective effect. Benzimidazole (CLXXIV) and 2-naphth-1'-ylmethylimidazoline (CLXXV)—the latter is the well known medicinal Naphthisin—are just as active[143].



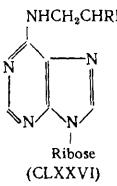
(CLXXIII)

(CLXXIV)

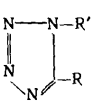


(CLXXV)

It has been reported that diphenylhydantoin improves the radiation resistance of mice[144], and that 3-hydroxypyridine derivatives have high protective activity[145].



(CLXXVI)



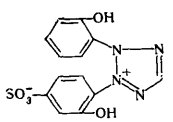
(CLXXVII)

a R=H, R'=ClC$_6$H$_4$;

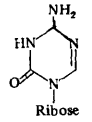
b R=NHNH$_2$, R'=Ph

Interesting results were obtained for the protective action of 6-substituted adenine ribosides (CLXXVI)[146]. In small doses compounds of this type with various substituents in the ethylamino-chain (R = H, CH_3; R' = CH_3, OH, NH_2, SH, CH_2NH_2, CH_2OH) show a well defined effect against radiation. Ribosides of 6-hydrazino- and 6-methylthio-purines were inactive, as were analogues

(CLXXVI) having the ethylamino-chain at position 8 in the ring system.



(CLXXVIII)



(CLXXIX)

Action against radiation has been observed also among tetrazoles. The most active were 1-chlorophenyl derivatives (CLXXVIIa), as well as 5-hydrazino-1-phenyltetrazole (CLXXVIIb)[146] and 2-*o*-hydroxyphenyl-3-2'-hydroxy-4'-sulphophenyltetrazole (CLXXVIII).

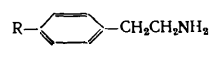
Czech workers[147] showed that certain aza-derivatives of pyrimidine have a protective effect in small doses. The highest survival rate of mice (55%) was observed with 5-azacytidine (CLXXIX) introduced 24 h before irradiation. The protective action was attributed[147] to a favourable effect on the proliferation of the stem cells responsible for repopulating bone marrow.

Protective action has been reported for thiamine[148], which contains pyrimidine and thiazole rings, derivatives of tetrahydropteridine[149], and haematoporphyrin[150].

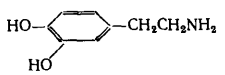
V. COMPOUNDS OF DIVERSE STRUCTURE

Amino-compounds

Protective action has been reported[151] in propylenediamine and in 2-methylpropylenediamine. *p*-Alkoxyphenylethylamines (CLXXX) exhibit activity against radiation[152], which diminishes with increase in the length of the hydrocarbon chain from C_4 onwards. The most active was *O*-methyltyramine (CLXXXa), which in an intraperitoneal dose of 50 mg kg^{-1} gave survival rates of 47–75% of irradiated mice (dosage rate 400–600 rad min^{-1}). Oral administration of this compound protects up to 40% of animals. The protective activity disappears when one or two amino-hydrogen atoms are replaced by alkyl or acyl. Il'yuchenko et al.[153] found that *O*-methyltyramine has the average action against radiation when mice are irradiated at rates of 2400, 216, and 65 rad min^{-1}, and they investigated the prophylactic protective activity of tyramine and its *O*-alkyl derivatives when mice were exposed to 10 rad min^{-1}. Under these conditions the *O*-pentyl and *O*-dodecyl derivatives (CLXXX: R = $C_5H_{11}O$, $C_{12}H_{25}O$) were more effective.

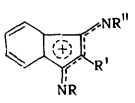


(CLXXX) a R=MeO

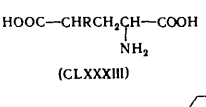


(CLXXXI)

Detailed investigation of the prophylactic protective action of dopamine (CLXXXI) showed[154] that a dose of 100 mg kg^{-1} protects ~ 60% of irradiated mice.



(CLXXXII)

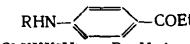


(CLXXXIII)

R = F, Et_2NCH_2–, , $(HOCH_2CH_2)_2N$–

Salts of 1-amino-3-iminoind-2-enes (CLXXXII) diminish the genetic damage in *Drosophila* caused by irradiation[155].

Protective activity was observed in certain γ-substituted glutamic acids (CLXXXIII)[84].



(CLXXXIV) a R=H, b R=OH

The study of analogues of *p*-aminopropiophenone (CLXXXIVa) has continued during recent years. *p*-Hydroxyaminopropiophenone (CLXXXIVb), a possible metabolite of (a), possesses approximately the same protective effect[156]. Vladimirov et al.[157] studied several aminopropiophenone and aminobenzophenone derivatives (Table 12), and showed that the action of most of them against radiation was directly dependent on their ability to form methaemoglobin, which requires the presence of a free amino-group in the molecule. These compounds include substances with a moderate protective action without causing the development of methaemoglobinaemia in the animals. Table 12 lists some of the most active compounds of this type.

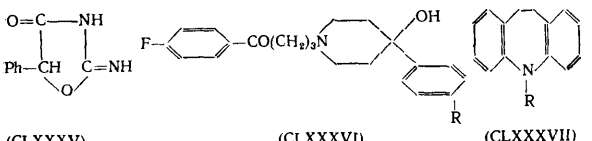
Table 12. Protective properties of aminopropiophenones[157].

Compound	Dose, mmole kg^{-1}	Survival, %
CLXXXIV a	0.2	60
CLXXXIV b	0.2	65
p-$H_2N-C_6H_4C(=NOH)Et$	0.25	60
o-$H_2N-C_6H_4COEt$	1.5	45
p-$H_2N-C_6H_4COEt$	0.5	75

Intraperitoneal introduction of phenylhydrazine 5–8 days before irradiation of mice resulted in a high survival rate[158].

Psychotropic Agents

These agents include compounds of diverse chemical structure exerting a prophylactic effect against radiation and those which are psychotropic medicinals. Slight protection is shown by the magnesium complex of Azoxodone (CLXXXV), a stimulant of the central nervous system[159]. The activity drops sharply in the absence of magnesium. Uray and his coworkers[160,161] studied the protective activity against radiation of tranquilisers of the Haloperidol series (CLXXXVIa). Intravenous injection of one of these preparations—Movotren (CLXXXVIb), which contains *p*-tolyl instead of a *p*-chlorophenyl substituent—into mice after 30 and 60 min protects up to 60–70% of the animals. The same workers[162] discovered that antidepressants—Imipramine and Trimipramine (CLXXXVIIa, b)—are able to increase the survival rate of irradiated mice.



(CLXXXV)

(CLXXXVI) a R=Cl, b–R=Me

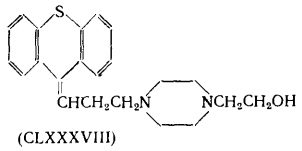
(CLXXXVII) a R=$-CH_2CH_2CH_2N(Me)_2$ b R=$-CH_2CH(Me)CH_2N(Me)_2$

According to Locker et al.[163,164] certain thymoleptics of phenothiazine and thioxanthen structure develop a marked

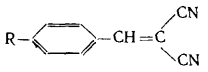
protective effect against radiation, which is strongest with Sordinol (CLXXXVIII). The effectiveness of this preparation was found to increase up to a certain limit with increase in the time between administration and irradiation.

Various Compounds

Among the > 40 nitriles and isothiocyanates studied, only the malononitrile derivative (CLXXXIX) exhibited a weak protective action in experiments on mice[165]. Activity against radiation was shown by diphenylmethanol derivatives with dimethyl- and diethyl-amino-groups in one and two benzene rings[166] and by 1-hydroxy-2-dimethylallylmethylamino-4-butylphenol[167]. *cis*-Dichlorodiammineplatinum develops a protective action in small doses: introduction into mice 1 and 24 h before irradiation produced a survival of 70%.[168]



(CLXXXVIII)



(CLXXXIX)
R=H, OH, Cl

Summarising, we may conclude that a vigorous search for protective agents against radiation has been made during the past 5–6 years among compounds of diverse structure. Most of the almost 1500 substances studied were sulphur-containing compounds, predominantly of amino-thiol structure. Considerable progress has been made during these investigations, the most important advances being listed below.

1. Compounds of high activity against radiation under the experimental conditions and possessing great therapeutic latitude have been prepared.
2. Highly efficient protective agents for oral administration have been found under the experimental conditions.
3. Comprehensive information has accumulated on the influence of the chemical structure of various classes of compound on their protective activity.

The main result must be to confirm and to provide a firmer basis for the possibility and promise of chemical protection of the living organism from ionising radiation.

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Negative Ions of Tetrapyrrole Compounds

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The mechanism of the formation of negative ions of phthalocyanine, porphyrins, and their metal derivatives is discussed, together with the effects of the tetrapyrrole ligand and the metal atom on the properties of the ions. The nature of the metal has a significant influence on the electronic structure of the negative ion, and thus on its properties, in particular its protonation, photoelimination of an electron from the ion, and its catalytic activity. Photodetachment of an electron combined with the spectral characteristics of the ions is considered as a method for investigating ionic forms. The Review concludes with a list of 132 references.

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I. INTRODUCTION

Ideas on intermolecular charge transfer in organic systems and on the properties of ions of aromatic compounds developed in a comparatively orderly sequence: extensive experimental results fitted well into the framework of theoretical concepts, quantum-mechanical calculations consistent with observation were made for the simplest and most characteristic cases, and comprehensive reviews and monographs were written[1-13]. The structural features of porphin molecules—the presence of heteroatoms and a tetrapyrrole ring of conjugated bonds, high symmetry, the possibility of coordinating a metal atom into the molecular structure—combined with the well known role of certain naturally occurring members of the series in biochemical processes have invariably attracted the attention of research workers to charge-transfer phenomena involving porphin derivatives. However, it is these structural features, which are obviously responsible for the extraordinary variety of properties of porphin derivatives, that make their investigation difficult and prevent the application to them of the general ideas developed from the examination of ions of aromatic compounds. Without considering all aspects of the problem we shall make a preliminary summary of researches on the negative ions of some of the simplest porphyrins. We shall not make a systematic survey of all the relevant literature but shall reply predominantly on recent results, which are relatively free from the errors and discrepancies inevitable in the early work.

The negative molecular ion Por^{n-} is formed from the neutral molecule Por of a porphin derivative by the successive addition of electrons. These ions can be generated by the same methods as the anions of aromatic compounds [2,6,9]. A chemical method is most often adopted, by introducing into the solution as electron donor either an alkali metal or an anion formed by its interaction with an aromatic compound possessing a smaller electron affinity than the porphin molecule. Almost 100% yields of anions have been obtained by this method from phthalocyanine, several porphyrins, and their metal derivatives. Good results are obtained by the electrochemical method, equally applicable to the generation of negative and of positive molecular ions. The method is almost indispensable when alkali-metal ions must not be present.

The first experiments on negative ions of porphins were made by Shablya and Terenin, who measured the electronic absorption spectra of the monoanions formed when magnesium phthalocyanine was treated with sodium in oxolan [14,15]. Almost simultaneously Watt and Dawes [16] examined by X-ray diffraction the products formed by copper phthalocyanine with potassium in liquid ammonia. These workers said nothing about the ionic character of the products, although now, of course, this is not open to doubt. The investigations were subsequently extended to anions of other metal phthalocyanines, and also to metal tetraphenylporphins and metal aetioporphyrins. In spite of several correct observations and conclusions in the early papers, the latter were often contradictory, which can be attributed to unavoidable errors due to the absence of reliable criteria of the purely ionic character of the reduction products of tetrapyrrole compounds, criteria of their purity, and reliable methods for identifying them. A difficulty in identifying and investigating tetrapyrrole anions was that electron spin resonance—one of the main methods for investigating ions of aromatic compounds—provided relatively little information. The e.s.r. spectra of tetrapyrrole anions are usually narrow singlet lines devoid of hyperfine structure [17-21]. In the few cases in which structural e.s.r. spectra were obtained [22-24] their interpretation gave rise to difficulties. Nevertheless, detection of a structureless e.s.r. signal is useful as proof of the radical (though not necessarily ionic) nature of the product, and is regarded as evidence of delocalisation of the electron in the conjugated system of the tetrapyrrole ligand [18]. Many uncertainties and contradictions were removed by a series of investigations in which spectral examination of negative tetrapyrrole ions *during their formation* were immediately followed by experiments on the photochemical detachment of an electron from the resulting ions [20,21,25,26].

II. PHOTOCHEMICAL DETACHMENT OF AN ELECTRON FOR THE STUDY OF NEGATIVE IONS

Like anions of aromatic compounds [27] those of tetrapyrrole derivatives are able to eliminate electrons photochemically [25]:

$$Por^{n-} \xrightarrow{h\nu} Por^{(n-1)-} + e^{-} .$$

This process converts a molecular anion either into an anion of smaller charge or (when $n = 1$) into a neutral molecule. For example, ultraviolet exposure of a solution of magnesium phthalocyanine monoanions in a mixture of oxolan and diethyl ether at −196°C (this mixture freezes as a transparent, vitreous mass) converts them into neutral molecules, which can easily be followed from the variation in the absorption spectra: disappearance of the bands due to the monoanion and the appearance of those due to the neutral molecule are accompanied by the appearance of a characteristic broad band with its maximum at 1240 nm, corresponding to electrons detached from the monoanions and stabilised in intermolecular potential traps in the matrix [28].

Photoelimination of an electron from an anion is reversible: when the frozen solution melts, the stabilised electrons escape from the traps and charge the molecules to the original level. The reverse reaction can also be achieved photochemically by illuminating the frozen specimen in the region of absorption by the stabilised electron ($\lambda > 700$ nm). Such exposure results in complete disappearance of the band due to the stabilised electron, but only a proportion of the electrons liberated from the traps add to magnesium phthalocyanine molecules. Some of the electrons probably fall into deeper traps, in which they do not exhibit their own absorption bands (at least in the experimentally accessible spectral region). Electrons captured in such traps also escape when the specimen melts, add to magnesium phthalocyanine molecules, and charge the latter to the original level.

Photoelimination of the first electron from a multicharged ion usually requires a smaller light quantum than does photoelimination from a monoanion. However, complete discharge of the magnesium phthalocyanine dianion to the neutral molecule is far more difficult than discharge of the monoanion. Detachment of the first electron obviously results in a net positive charge in the matrix cell formed by the molecular anion, the positive gegenions interacting with it, and the solvate sheath surrounding them, and it is now considerably more difficult to remove a second electron. Tetra-anions of certain metal phthalocyanines split off the first electron even under the influence of visible light, ultraviolet exposure gives dianions, but no further photoelimination of electrons is observed. These experiments indicate that the matrix potential traps in which the photoeliminated electron is located lie outside the ionic association complex comprising the anion, positive gegenions, and the solvate sheath surrounding them.

Photorelease of an electron has been observed also in other vitreous matrices, e.g. in an equimolecular mixture of oxolan and dimethylformamide. Here the photodischarge of ions was not accompanied by the appearance of a band due to the stabilised electron, and the reverse reaction occurred only when the specimen was thawed [26]. The liberated electrons may be localised in intramolecular traps due to the presence of vacant molecular orbitals in the dimethylformamide molecules.

Photodetachment of an electron, similar to that described above for multicharged magnesium phthalocyanine anions, has been observed also with negative ions of several other metal phthalocyanines and metal porphyrins [20,21,25,26].

The appearance of stabilised electrons in the matrix accompanied by formation of neutral magnesium phthalocyanine molecules when monoanions are irradiated is sufficient proof that these monoanions are a purely ionic species, differing from the neutral molecules only in the presence of an additional electron. The purely ionic structure of multicharged magnesium phthalocyanine ions is proved by a comparison of the absorption and e.s.r. spectra of products of successive stages of one-electron reduction and their photochemical discharge.

More detailed investigations have established several special features of the photodetachment of an electron [26]. The longer-wavelength threshold of photodetachment

differs markedly with ions of different compounds. Impurities can be distinguished and sometimes identified from the absence of synchrony in the variation of absorption bands on photoelimination of an electron. Thus this phenomenon will give the missing proof of the ionic character of products of the reduction of tetrapyrrole compounds by alkali metals, and will yield reliable spectral characteristics for their identification and analysis.

A method of photoinduced dichroism is based on the photoelimination of an electron. It enables both the relative positions of the molecular oscillators in the anion (polarisation of electron transitions) and their distribution relative to those of the neutral molecule to be determined [29-33]. Such results are important for interpreting the electronic absorption spectra of the anions.

The essence of photoinduced dichroism is that, if a photochemical reaction (in the present case photoelimination of an electron from negative ions in a frozen solution) takes place in an isotropic solid medium under the influence of plane-polarised light, the medium becomes dichroic, since molecules (ions) appropriately oriented relative to the electric vector of the plane-polarised light are preferentially subject to photoconversion. Photoinduced dichroism lasts for a fairly long time in a frozen matrix, and it becomes possible to determine the spectral dependence of its characteristic parameter $\Delta D = D_{\parallel} - D_{\perp}$, where $D_{\parallel}$ and $D_{\perp}$ are the optical densities of the specimen measured in light polarised respectively parallel and perpendicular to the direction of polarisation of the light causing the photoreaction. If only three mutually perpendicular directions of polarisation of electronic transitions are possible owing to symmetry in the molecules (ions) (as occurs with porphyrins, phthalocyanine, and their metal derivatives), the direction of polarisation of transitions corresponding to absorption bands both of the starting material and of the photoreaction product can be determined in a coordinate system coincident with the molecular axes of symmetry. For this it is usually sufficient to determine the sign of ΔD in the given absorption band. This method has been used to determine the orientation of the dipole moments of electronic transitions in the monoanions of disodium complexes of chlorin and tetraphenylbacteriochlorin with respect to transitions of the neutral molecules (in a coordinate system unique to the molecule and the ion) [32,33].

III. ELECTRONIC STRUCTURE AND THE SPECTRA OF NEGATIVE IONS OF METAL PHTHALOCYANINES

The most detailed investigations have been made on the negative ions of metal phthalocyanines. Kholmogorov and Shablya [18] were the first to measure the e.s.r. spectrum of magnesium phthalocyanine monoanions and, from the form of the structureless narrow signal, suggested that the extra electron was delocalised over the cyclic conjugated-bond system of the tetrapyrrole ligand. Taube and his coworkers showed [34-41] that a metal phthalocyanine molecule may add successively 1–4 electrons on reaction with an alkali metal or with a benzophenone anion. They measured the magnetic susceptibility of the ions, made an elementary analysis of them, undertook LCAO-MO calculations to determine the electronic configurations of the metal phthalocyanine monoanions, and also studied the Mössbauer spectra of iron phthalocyanine anions. Unfortunately, none of their papers gives either optical or e.s.r. spectra. This omission makes it difficult either to compare the results with those of other workers or to reproduce them. Use of such a simple method as molecular orbitals for theoretical calculations of electronic configurations of complicated species containing transition-metal atoms is open to sceptism. In almost every individual case the calculations must be confirmed by experiment, which larely deprives the calculations of their predictive value. A recent attempt [42] to interpret the spectra of the mono-, tri-, and tetra-anions of magnesium phthalocyanine on the basis of calculations by the Pariser–Parr–Pople method, allowing for limited configuration interaction, omitted calculation of the intensities of the electronic transitions. Furthermore, agreement between calculated and experimental spectra of the mono- and trianions was obtained only on the hypothesis that the band of longest wavelength does not correspond to the transition of lowest energy among those predicted as allowed. There are no experimental grounds for such a hypothesis. Therefore the interpretation of the electronic spectra of the ions given by these workers cannot be accepted as reliable. Thus at the present stage theory plays only an ancillary part in relation to tetrapyrrole ions, and all the main conclusions, being based on a comparison of experimental results, are predominantly qualitative in character.

The problem in the electronic structure of metal phthalocyanine ions is essentially the location of the added electrons, since the nuclear configurations of ions and neutral molecules can be regarded to a first approximation as the same. The excess charge of the anion can in principle be located either on the central atom M or on the tetrapyrrole ligand, or shared between them in certain proportions. The hypothesis that the charge of the magnesium phthalocyanine monoanion is located on the ligand, which was based on e.s.r. data [18], has since found direct experimental confirmation in the close similarity between the electronic absorption spectra of the monoanions of magnesium and of metal-free phthalocyanines [43-45]. Comparison of the results of absorption spectroscopy, e.s.r. spectroscopy, and theoretical calculations shows that the electron is also located on the ligand in the monoanions of zinc, copper, and nickel phthalocyanines [19,22,23,37,43-48]. The monoanion of cobalt phthalocyanine has a different structure: although it is diamagnetic and therefore inaccessible to e.s.r. investigation, the close similarity of the electronic absorption spectra of the complex and its monoanion is sufficient to suggest that the electron is located on the cobalt atom in the latter [44,48,49]. The energy states of the principal chromophore of the molecule—the tetrapyrrole ligand—show little change, and the spectrum of the monoanion retains the main features of the neutral molecule. (Addition of an electron to the magnesium, copper, and nickel phthalocyanine molecules leads to significant spectral changes.) Taube's calculations [37] support the postulated location of the electron in the monoanion of cobalt phthalocyanine based on spectral data.

The absorption spectra of the dianions of metalfree, magnesium, nickel, and copper phthalocyanines, like those of the monoanions, depend little on the nature or even the presence of the metal atom in the molecule. This means that both electrons in the dianions are located in the tetrapyrrole system of the ligand [44-46,48]. The absorption spectra of cobalt phthalocyanine dianions are closer to those of the monoanions than those of phthalocyanine dianions (and the analogous metal phthalocyanine dianions). It may be assumed, in agreement with calculation, that one electron is located on the cobalt atom, and the other on the ligand.

The electronic structure of the monoanion of iron phthalocyanine may be considered separately. According

to Taube [37] the location of the extra electron in a metal phthalocyanine anion depends on the electronegativity of the metal atom. Thus nickel is the most electronegative of the iron-group metals, and in conformity with this its atom remains unchanged when its phthalocyanine complex is converted into a mono- or a di-anion, since both electrons are located on the ligand. Cobalt is intermediate in electronegativity, so that on reduction of its phthalocyanine complex the first electron goes to the cobalt atom, and the second to the ligand. Since the iron atom is the least electronegative, both electrons should be located on the iron atom when the phthalocyanine complex is reduced. However, the properties of a metal atom, including its electronegativity, may obviously change on coordination into the tetrapyrrole molecule. The absorption spectra of iron phthalocyanine anions show [49] that their electronic structure does not fit a simplified theoretical scheme: the spectrum of the monoanion in oxolan alone or mixed with diethyl ether differs both from that of the cobalt monoanion with its electron on the metal atom and from that of the nickel monoanion with a negatively charged ligand. It was suggested that the negative charge is shared between the iron atom and the ligand. In quantum-mechanical terms this may imply e.g. that the electron is located on a d-level of the iron atom, which is strongly mixed with a vacant π-electron level of the ligand as a result of their proximity. This suggestion has found experimental support, including aspects of the photodetachment of electrons from monoanions of various metal phthalocyanines. Ultraviolet exposure easily detaches the electron from the nickel phthalocyanine monoanion, in which it is situated on the ligand. Detachment of the electron does not occur with the complex cobalt monoanion. Iron phthalocyanine monoanion occupies an intermediate position: although photoelimination occurs, far more work is required than with the complex nickel anion.

Convincing evidence for the suggested location of charge in the iron phthalocyanine monoanion is given by the phenomenon of thermochromism which we have discovered with these ions [26,49]. In solution at temperatures close to $-196°C$ these ions are able to form unstable complexes with molecules of organic bases (pyridine, N-methylpiperidine, diethylamine, triethylamine), which decompose with rise in temperature and are re-formed on subsequent cooling. The changes in temperature are accompanied by changes in colour—blue at $-196°C$, but red at $-100°C$ and above (thermochromism). The absorption spectrum of the red solution is identical with that of iron phthalocyanine monoanion in the absence of bases. However, the spectrum of the blue solution, in which the ions are present as complexes with the molecules of bases, become similar in detail to that of the monoanion of nickel phthalocyanine, in which the negative charge is located on the ligand, as already stated. The molecules of the base, being oriented with their dipoles directed towards the iron atom on formation of the complex with iron phthalocyanine monoanion, obviously make complete localisation of the extra electron at the π-electron level of the ligand energetically favourable. Such a phenomenon would hardly have been possible if the electron were located on the metal atom; in any case, the presence of bases in solution produces no spectral changes in cobalt phthalocyanine ions involving localisation of the electron on the metal atom. As was to be expected, the iron phthalocyanine monoanion in the complex with a molecule of a base, while having the extra electron on the ligand, eliminates it on exposure just as easily as does the monoanion of nickel phthalocyanine.

A recent investigation of the Mössbauer spectra of the singly and doubly charged anions of iron phthalocyanine also indicates some distribution of negative charge between ligand and metal atom in these ions. These results were explained in terms of mixing of the d-orbitals of the iron atom with the π-orbitals of the ligand [40,41].

A point in connection with terminology and the nature of the problem is that it was supposed in some of the early publications [16,35] that the reduction of a metal phthalocyanine (MPhth) involves a change in valency ("state of oxidation") of the central metal atom. This was represented by such notation as

$$Co^{II}\,Phth \xrightarrow{e^-} Co^{I}\text{-}Phth;$$

$$Fe^{II}\text{-}Phth \xrightarrow{e^-} Fe^{I}\text{-}Phth \xrightarrow{e^-} Fe^{0}\text{-}Phth.$$

Watt and Dawes supposed [16] that the initial product of the reduction of copper phthalocyanine CuPhth by potassium is $Cu^{I}Phth$, followed by $Cu^{0}Phth$, the copper atom in the latter being coordinated with the ligand, not combined covalently. The results discussed above show that in actual fact the copper atom in the phthalocyanine complex plays no decisive part in the addition of electrons. Even when the electron is actually located on the metal atom, as in the formation of $[CoPhth]^-$, there are no grounds for assuming that this involves a change in the valency of the cobalt atom or the nature of its bond with the ligand. It would therefore be logical to cease denoting the primary reduced form of cobalt phthalocyanine by the formula $Co^{I}Phth$, as is done even now in certain papers, and to use the formula $[CoPhth]^-$ or even, when the location of the charge is to be emphasised, the formula $[Co]^-Phth$. Analogous notation should be used also for negative ions of all other tetrapyrrole compounds.

The problem of the electronic structure of multicharged metal phthalocyanine ions has been solved only in general outline. Absorption spectroscopy, e.s.r. spectroscopy, and electron photoelimination have shown that the molecules of most metal phthalocyanines are able to add successively up to four electrons with the production of purely ionic forms [25,26]. The possibility of adding such a number of electrons is attributed to the doubly degenerate lowest vacant π-orbital in the metal phthalocyanine molecule [47]. The presence of the central metal atom with a more or less independent system of energy levels also permits the addition of extra electrons. It is assumed, for example, that an additional vacancy on the cobalt atom makes it possible for cobalt phthalocyanine to exist in five negatively charged ionic forms [37,48]. We have previously cast doubt [44] on the existence of the fifth ionic form. Recently we have been able to obtain a fifth reduced form of this compound, having the same absorption spectrum as given by Clack and Yandle [48]. In contrast to most other $[MPhth]^{n-}$ ions investigated, including tri- and tetra-anions of cobalt phthalocyanine, however, this fifth reduced form was incapable of photoelimination of an electron, which gave serious grounds for doubting whether it actually had a purely ionic structure.

Calculations by the LCAO-MO method showed [36-41,47,50] that the third and fourth electrons added to a metal phthalocyanine molecule to form tri- and tetra-anions should be located in a doubly degenerate π-electron level of the ligand. However, experimental studies of the Mössbauer spectra [40,41] and electronic absorption spectra [44] suggest that the charge in multicharged metal phthalocyanine ions is distributed between the metal atom and the ligand. The close similarity of the absorption spectra of tetra-anions of different metal phthalocyanines (magnesium, nickel,

cobalt, iron) shows that the charge distribution in them is little affected by the nature of the metal.

Clack and Yandle assume that the presence of paramagnetism in trebly charged magnesium phthalocyanine anions indicates that all three extra electrons are located on the ligand. The corresponding cobalt complex anion has similar electronic absorption spectra and hence the same electronic configuration[48]. Thus these workers conclude that, on passing from the doubly to the trebly charged cobalt phthalocyanine anion, not only does the third electron add to the ligand, but the electron located on the metal in the singly and doubly charged anions also passes to the ligand. Such a phenomenon can actually result from change in the relative positions of the π-orbitals of the ligand and the d-orbitals of the metal atom when an electron is added to the system, where the raising of the d-orbitals should exceed that of the π-orbitals. As yet, however, such a change in the relative positions of the orbitals has neither a theoretical nor an experimental basis. It is more reasonable to postulate that the π-orbitals undergo a greater rise than do the d-orbitals on addition of an electron, and that localisation of the electron in the d-orbitals will become possible at some stage. Such a process can be assumed in the formation of trebly charged anions of magnesium and similar metal phthalocyanines, and it is then easy to explain the spectral similarity of the trianions of magnesium and cobalt phthalocyanines: they have the same electronic configurations, with (the larger) part of their charge located on the ligand, and the other part on the metal atom.

Without analysis of the structure of the e.s.r. spectra neither the presence nor the absence of paramagnetism will give any information on the location of the charge in an anion. For example, the unpaired electron in the paramagnetic copper phthalocyanine molecule is located on the copper atom, and the extra electron of the singly charged anion on the ligand, but, despite such spatial separation of the electrons, the monoanion as a whole is diamagnetic. The trebly charged magnesium phthalocyanine anion must be assumed to be paramagnetic independently of the location of the extra electrons, since they are distributed within a single system of energy levels.

Peculiarities may be noted in the behaviour of certain metal phthalocyanines on conversion into negative ions. The metal-free compound reacts with sodium to give a disodium complex, which can be reduced to ionic forms analogous in spectra and structure to those of the magnesium and zinc complexes[47]. Singly and double charged phthalocyanine anions could be obtained and examined spectroscopically during the photochemical reduction of phthalocyanine by hydrazine[43]. Copper in its phthalocyanine complex has a tendency to be replaced by sodium on reaction with the latter, but substitution occurs when the molecule adds a third electron. The optical and e.s.r. spectra of singly and doubly charged copper phthalocyanine anions indicate that their electronic structures are similar to those of the corresponding complex magnesium and zinc anions[46,47]. The replacement of copper by sodium at the third stage of reduction is indirect confirmation of the hypothesis that localisation of the charge on the metal atom takes place at this stage[44].

Manganese phthalocyanine, like the cobalt complex, yields five reduced forms on interaction with an alkali metal in oxolan[51]. The metal atoms in manganese and chromium phthalocyanines are able to change their valency easily and reversibly by adding various out-of-plane groups or molecules (hydroxyl, cyano, acetate, pyridine, etc.)[52]. This greatly complicates investigation of their ionic forms[26]. It was observed in particular that the reduction of chromium phthalocyanine by sodium in oxolan gives a paramagnetic product whose e.s.r. spectrum contains nine lines, which means that the unpaired electron interacts with the four inner nitrogen atoms. When the complex is reduced in hexamethylphosphoramide, a signal comprising seventeen lines is observed, which corresponds to interaction of the unpaired electron with the eight nitrogen atoms[23,53]. Such behaviour of chromium phthalocyanine is obviously due to a different distribution of electron density in the resulting ion, which depends on the out-of-plane ligand, as in the interaction of iron phthalocyanine monoanions with bases[49].

We have not hitherto specified how the charge is actually distributed in the tetrapyrrole system of the ligand. Yet this distribution determines the chemical properties of the ion. Unfortunately, theoretical and experimental information is at present insufficient to solve this problem. Published data can be found permitting comparison of the distribution of π-electron density in certain molecules and their ionic forms. For example, theoretical calculations showed that, on formation of the negative ion of tetracyanoquinodimethane, the π-electron density increased most strongly on those atoms on which it was highest even in the neutral molecule (on the cyano-nitrogen atom and on the carbon atom linking the cyano-group with the quinoid ring). In neutral molecules the π-electron density has its minimum value on the cyano-carbon atom. Subsequently it diminishes still more strongly (though slightly) on conversion of the molecule into the singly and doubly charged anions[54,55]. In just the same way the increase in charge density on a carbon atom accompanying formation of radical-anions of polyacenes is greater the higher the π-electron density on the atom in the neutral molecule[56,57]. The physical reason for such a charge distribution in a negative molecular ion is obviously that the added electron, merging with the π-electrons of the neutral molecule, obeys the same distribution laws as do the latter in the force field of the given atomic configuration, which changes little on transformation of the molecule into an ion.

It may be supposed as working hypothesis, by analogy with polyacenes and tetracyanoquinodimethane, that the charge of an electron added to a metal phthalocyanine molecule is distributed (if it is located on the ligand) mainly between both inner and outer nitrogen atoms, which in the neutral molecule bear a considerable excess charge relative to the carbon atoms of the benzene rings[58-61].

IV. NEGATIVE IONS OF PORPHYRINS AND METAL PORPHYRINS. PROTONATION OF NEGATIVE IONS

The structural features distinguishing metal porphyrins from metal phthalocyanines are responsible for the distinctive physicochemical properties both of their neutral molecules and of their ions. Negative ions could be obtained by the same methods as those of the latter, but significant differences between them were immediately discovered: metal porphyrins form only singly and doubly charged anions, although their lowest vacant π-orbital is doubly degenerate, as in metal phthalocyanines, and the addition of four electrons is formally possible[50]. Reports of the formation of more highly charged ionic forms[17,22,62-64] have since been disputed. Experiments on the photodetachment of an electron and on the protonation of ions have shown[20,25,26,65,66] that partly protonated multicharged anions had erroneously been

regarded as purely ionic forms. It is not yet clear why metal porphyrins do not form multicharged ions.

As with metal phthalocyanines, the formation of negative ions of metal porphyrins and their structure depend significantly on the presence and on the nature of the central metal atom. Porphyrins and their copper derivatives resemble phthalocyanine and copper phthalocyanine in being converted into disodium complexes at the first stage of interaction with alkali metals or with negative anthracene ions, and these complexes yield ionic forms at later stages [46,64]. This transformation slows down with fall in temperature, and both monoanions and dianions could be obtained by running together solutions of a porphyrin (aetioporphyrin or tetraphenylporphin) and singly charged anthracene anions at −70°C. [26,64,67] An electrochemical method can also be used to obtain and investigate negative ions of metal-free porphyrins [68-70].

Zinc and magnesium combined with porphyrins are not replaced by alkali metals, and their valency is not changed by redox reactions, so that the first successful experiments on the preparation and spectral investigation of ions of metal porphyrins were made with zinc tetraphenylporphin by Closs's method [17,62]. Later experiments [20,26] with photodetachment of an electron from anions of this complex confirmed the correctness of the spectral characteristics predicted for these anions.

The close similarity of the electronic absorption spectra of the singly charged anions of tetraphenylporphin and its zinc complex, which contain comparatively few bands and, it may be said, are unique [67-70], demonstrate, when combined with e.s.r. measurements [17,19,20,22] and theoretical conclusions [50], that the extra electron is delocalised in the cyclic bond system of the tetrapyrrole ligand. Charge is similarly distributed in the singly charged anions of metal-free, zinc, magnesium, and disodium aetioporphyrins and of metal-free, copper, tin, magnesium, and disodium tetraphenylporphins. The second electron in the doubly charged anions of aetioporphyrin, tetraphenylporphin, and their zinc, magnesium, and copper derivatives is probably also located on the ligand, although the only evidence is a comparison of the absorption spectra of the doubly charged anions of porphyrins and of their metal derivatives. Cobalt and iron atoms introduce a significant anomaly into the charge distribution in the ions of metal porphyrins. Many experimental results indicate that the negative charge in the monoanion of cobalt tetraphenylporphin is located on the cobalt atom [19,71,72]. Information is lacking on products of the further reduction of cobalt porphyrins. Hush and Woolsey report [73] that, when an analogue of cobalamin is reduced with sodium, the first electron is located on the cobalt atom, but on addition of the second electron the whole of the excess charge shifts to the ligand. On formation of singly and doubly charged anions of the corresponding nickel complex both electrons are localised on the ligand. These conclusions were based on a comparison of the absorption spectra of ionic forms and the neutral molecules of the compounds.

Iron porphyrins occupy a special position among other metal porphyrins by virtue of their exceptional capacity for complex formation with out-of-plane ligand molecules and the readiness with which the state of the iron atom changes between bivalent and tervalent. The metal atom in iron(III) porphyrins binds outside the plane of the tetrapyrrole ring with CN, OH, Cl, etc. This ability of iron derivatives of the porphin series, which is responsible for the important part played by individual representatives in biological processes and on which numerous publications have appeared, greatly complicates investigation of their ionic forms. According to spectral data the first stage of interaction between ClFe^{III}AeP and negative pyridine ions is reduction of the central iron atom to the bivalent state [64]. Subsequent stages of this interaction are dissimilar in spectral characteristics from the changes undergone by other metal aetioporphyrins under the same conditions, and no data are yet available on the structure of the ionic forms of iron aetioporphyrin. Three reduction products have been characterised spectroscopically when oxybis[iron(III) tetraphenylporphin] (two molecules of the iron complex bound by an oxygen atom between the iron atoms) is treated with sodium amalgam in oxolan. The first stage is assumed to involve formation of a singly charged iron tetraphenylporphin anion with localisation of the charge on the metal [72].

Singly charged anions and cations of many metal derivatives of octaethylporphin have been obtained by electrochemical reduction. The potentials at which addition or removal of an electron takes place have been measured. Comparison of the absorption spectra of ionic forms and neutral molecules indicated whether the ionic charge was located on the metal atom or on the ligand [74]. Metals which are not involved in redox reactions when present in octaethylporphin complexes (the whole of the ionic charge is localised on the ligand) include alkali and alkaline-earth metals, the bivalent metals palladium, copper, zinc, and cadmium, tervalent antimony, scandium, aluminium, gallium, indium, and thallium, quadrivalent silicon, germanium, and tin, and also the metals present in vanadyl and titanyl. Among metals which change their valency under these conditions are—(*a*: I ⇌ II) cobalt; (*b*: II ⇌ III) manganese, iron, cobalt, chromium, and silver; (*c*: II ⇌ IV) lead; (*d*: III ⇌ IV) chromium and iron; and (*e*: IV ⇌ V) molybdenyl—where a metal atom undergoes a real change in valency only when a redox reaction involves a change in the number of atoms with which it forms valency bonds. If this number remains unchanged [as in the interconversion of cobalt(I) and cobalt(II) porphyrins], it is preferable to regard this as a change not in valency but in the population of the orbitals of the metal atom.

An interesting distinction between the ions of metal porphyrins and those of metal phthalocyanines is the enhanced tendency of the former to protonation. Slight contamination with proton-donating impurities (alcohols, weak acids) may result in conversion of the ionic forms of a metal porphyrin into partly or completely protonated ionic forms [17,20,25,26,66,68,69,75]. The protonation of doubly charged anions is represented by the scheme

$$Por^{2-} \xrightarrow{H^+} PorH^- \xrightarrow{H^+} PorH_2$$

(where Por represents a molecule of a neutral tetrapyrrole compound).

Products of the protonation of zinc tetraphenylporphin ions obtained by this method [20] were identical in absorption spectra and other properties with products of the photochemical reduction of the complex by hydrazine [76]. Protonation of doubly charged zinc aetioporphyrin anions follows by removal of zinc atoms from the protonated ions yielded reduced products spectrally identical with products of the photochemical or dark reduction of metal-free porphyrins to the corresponding dihydro-derivatives [77]. This gave independent confirmation of the structure of the photoreduced forms of porphyrins and their metal derivatives, while the reduction of a metal porphyrin to its hydrogenated form was separated experimentally into two stages: primary addition of an electron was followed by protonation of the resulting negative molecular ion.

The form $PorH^-$ can be obtained in an oxolan solution of zinc aetioporphyrin anions by reaction of Por^- or Por^{2-} with a comparatively weak proton donor, e.g. methanol. The monoanion Por^- is converted into $PorH^-$ by disproportionation:

$$2\,Por^- + H^+ = PorH^- + Por\ .$$

Interaction with a strong proton donor—acetic acid—yields the dihydro-derivative[66]. Protonation of the anions of metal porphyrins leads, of course, to significant changes in their spectral characteristics: the electron delocalised in the tetrapyrrole system of the ion becomes localised near the added proton, forming a valency bond with it. If the proton adds to a methine bridge, as is assumed to occur, the cyclic conjugation in the tetrapyrrole system will break down, and the whole system of energy levels will change. Addition of a second proton will lead to further spectral changes[20,66].

It proved impossible to effect photoelimination of an electron from the forms $PorH^-$ and $PorH_2$. Nor were attempts to obtain neutral radicals PorH· by the protonation of monoanions successful.

Partly protonated ionic forms $PorH^-$ of zinc and magnesium aetioporphyrins and tetraphenylporphins, like the neutral molecules, are able to add electrons on reaction with sodium, with the successive formation of $PorH^{2-}$ and $PorH^{3-}$. The first of these forms is paramagnetic and capable of photoelimination of an electron with regeneration of $PorH^-$, which is proof of its structure $[PorH^{2-}]$. In the presence of methanol the form $PorH^{3-}$, which can be termed a partly protonated trianion, is converted via a disproportionation stage into diamagnetic protonated tetra-anions, which exist in two spectroscopically distinguishable forms containing different numbers of excess protons[26,66].

The form $PorH_2$ is easily converted by loss of a proton into $PorH^-$, a reversible change governed by the acid–base equilibrium conditions. For example, a critical review, in the light of later results, of earlier work[76] on the photoreduction of zinc tetraphenylporphin shows that the presence of ammonia or hydrazine in pyridine solution leads to conversion of the dihydro-derivatives into the form $PorH^-$. Evaporation of the solution and dissolving the precipitate in pure pyridine again yields the $PorH_2$ form. In frozen solutions in organic bases a proton can be detached photochemically from the dihydro-derivative of zinc aetioporphyrin. The resulting $PorH^-$ form is again converted into $PorH_2$ when the solution melts[78].

Parly protonated anions and hydro-derivatives of metal porphyrins were repeatedly observed earlier in experiments on the dark and photochemical reduction of these compounds[76,79–84]. Successful attempts have recently been made to determine the structure of the products by nuclear magnetic resonance. Thus the added hydrogen atoms in the dihydro-form were shown to be situated on two opposite methine bridges, and in $PorH_3^-$ (or $PorH_4$) three of the four methine bridges were hydrogenated[84,85]. The form $PorH^-$ was regarded by the Closs's[17] on the basis of n.m.r. data as a metal phlorin, in full agreement with spectroscopic results.

In an optically excited state the capacity of negative ions of metal porphyrins for protonation is considerably increased, as is indicated by the possibility of accomplishing the photochemical protonation of metal aetioporphyrin ions in the presence of negative ions of pyridine. Here the pyridine ions act as proton donors, being converted into bipyridyl during the reaction[75].

Negative ions of metal-free porphyrins can also be converted into protonated forms. Experiments on the electrochemical reduction of tetraphenylporphin, the dimethyl ester of deuteroporphyrin, and the dimethyl ether of mesoporphyrin yielded not only singly and doubly charged anions but also the form $PorH^-$ having a phlorin structure, protonated tetra-anions $PorH_n^{(4-n)-}$ with a porphomethene structure, and protonated hexa-anions $PorH_n^{(6-n)-}$ with a porphyrinogen structure. The exact number of protons n in these forms was not determined[68,69]. Highly reduced colourless products formed from zinc aetioporphyrin by interaction with sodium had been observed earlier[63,64], probably containing six extra electrons and an unknown number ($n \leq 6$) of protons.

The protonated ions of porphyrins and of their metal derivatives exhibited closely similar absorption spectra at the same state of reduction. This similarity provides hints for determining the structure of the reduction products of porphyrins, in particular the location of hydrogen atoms added to the molecule.

Like porphyrins, their hydrogenated derivatives—chlorins and bacteriochlorins—are able to form singly and doubly charged anions. Negative ions of tetraphenylchlorin and tetraphenylbacteriochlorin have been obtained electrochemically and investigated by means of their absorption spectra[69]. In the presence of proton donors tetraphenylchlorin ions are converted into protonated forms: partly protonated dianions and protonated tetra-anions with an unknown number of protons have been recorded spectroscopically, but protonated hexa-anions are not formed by tetraphenylchlorin. In general the same final reduction product, porphyrinogen, is obtained from the tetraphenyl derivatives of porphin, chlorin and bacteriochlorin[65,69]. The bacteriochlorin molecule requires only two electrons and two protons for conversion into porphyrinogen, and the chlorin and porphyrin molecules require respectively four and six electrons and protons each. Partly protonated ions are intermediate stages in the reduction of these molecules to porphyrinogens.

Singly charged anions of disodium complexes of tetraphenylchlorin and tetraphenylbacteriochlorin have been obtained by the action of sodium on the metal-free compounds in dimethylformamide. They were proved to possess a purely ionic structure by photoelimination of an electron[32,33]. Singly charged anions of bacteriochlorophyll and of zinc tetraphenylbacteriochlorin were obtained by an electrochemical method[86]. The absorption spectra of the latter are similar to those of mono-anions of the corresponding disodium derivatives[33], which indicates that the extra electron is located on the ligand.

The effects of the central metal atom and of the charge distribution on protonation of the anion have not been investigated, although the charge distribution in the tetrapyrrole system of the ligand probably determines both the capacity of the ion for conversion into a protonated form and the structure of the latter (location of added protons). In support of the suggested role of the distribution of negative charge in an ion on its protonation we can consider the photochemical reduction of various metal phthalocyanines, involving as initial stage formation of a negative ion and a subsequent protonation stage. The ability of these complexes to form photoreduced varieties is substantially dependent on the nature of the metal. Magnesium and zinc phthalocyanines are converted into dihydro-derivatives when their pyridine solutions are exposed in the presence of hydrazine[87], whereas all cases investigated[44] of the photoreduction of cobalt phthalocyanine led merely to the formation of singly charged

anions $[CoPhth]^-$. Photoreduction of iron phthalocyanine has not yet been achieved[88]. These differences can be explained in terms of the electronic structures of the singly charged anions. In the magnesium complex ion the electron is located on the ligand, and a proton readily interacts with this ion to give a hydro-derivative, forming a valency bond with one of the outer nitrogen atoms. (It is on these atoms that the excess charge of magnesium phthalocyanine anions is presumably located.) A proton interacting with the complex cobalt anion is located near the cobalt atom, on which almost all the negative charge of the ion is situated; the conjugated system of the ligand remains unchanged, and the proton forms a purely ionic bond with the singly charged anion. The inability of iron phthalocyanine to be photoreduced can also be explained by peculiarities of the charge distribution in its monoanion (see above). We have recently been able to achieve the photoreduction of this complex in *N*-methylpiperidine by exposure to ultraviolet radiation at a low temperature, with formation of a photoproduct spectrally similar to the product of the photoreduction of magnesium phthalocyanine, and obviously also a dihydro-derivative. A possible explanation of the photoreduction of iron phthalocyanine is that the singly charged anion formed in the first stage of the photoreaction acquires in this medium an electronic structure with the charge localised on the ligand in virtue of the above redistribution of charge in the ion on formation of a complex with a molecule of a base.

Ions of metal phthalocyanines are not so sensitive as those of metal porphyrins to contamination with proton-donating impurities, and are protonated only at comparatively high concentrations of protons. Singly and doubly charged magnesium phthalocyanine anions are converted into the dihydro-derivative on treatment with acetic acid, as are the corresponding ions of metal porphyrins, but they probably retain their ionic structure in the presence of methanol, which leads merely to a change in the solvate sheath of the ions and to replacement of positive alkali-metal gegenions by protons, as is indicated by the comparatively small spectral differences. Nor can the possible formation of complexes between the metal phthalocyanine anion and the alcohol molecule be excluded. Such complexes have recently been discovered in experiments with fluorenyl anions[89]. Protonation of quadruply charged magnesium phthalocyanine anions by methanol or acetic acid yields new products, not yet identified, which may include both tetrahydro-derivatives and partly protonated tetra-anions[21].

V. PHOTOCHEMICAL GENERATION OF NEGATIVE IONS IN SOLUTION

The photochemical generation of ions not only supplements existing methods (chemical and electrochemical) but also gives indications of the reasons for the photochemical activity of molecules and the mechanism of the photo-transfer of an electron, the primary act in any redox reaction. Attempts were made long ago to obtain photochemically ionic forms of tetrapyrrole compounds, especially chlorophyll and its analogues, but only recently have positive results been obtained in isolated cases thanks to the development of methods for the spectroscopic identification of ions and to the selection of appropriate experimental conditions. The problem of the photogeneration and stabilisation of negative ions of porphyrins and their metal derivatives in liquid solutions is complicated by the high proton-accepting activity of these ions. When this property was established, the requirements of the medium in which they could exist became obvious—absence of those proton-donating and electron-accepting impurities causing oxidation of the ions and their discharge to neutral molecules, as well as adequate solvating power to stabilise the ionic forms.

One of the most suitable solvents for the photogeneration and stabilisation of anions of tetrapyrrole compounds was dimethylformamide with hydrazine added as reductant, provided that the reagents had been reliably freed from the above impurities. Almost complete conversion of magnesium phthalocyanine into stable singly charged anions could be achieved in this medium by exposure to visible light at $-50°C$.[43,90] Absorption and e.s.r. spectra showed that the photogenerated monoanions were identical with those obtained by interaction with alkali metals. Similar transformation on illumination occurred in this medium also with metal-free phthalocyanine. Ultraviolet irradiation of solutions of monoanions of phthalocyanine or its magnesium complex led to their further reduction to dianions[43].

Singly charged anions of magnesium phthalocyanines can be obtained in almost 100% yield also by exposing solutions of this complex in piperidine, which acts also as an electron donor. Radical-cations of piperidine could not be detected in the e.s.r. spectrum, probably owing to dimerisation of the cations or some other process leading to their neutralisation. In combination with the good solvating properties of piperidine as a solvent this ensures relatively high stability of the radical-anion of magnesium phthalocyanine in the liquid solution[91]. The presence of a proton donor—ascorbic acid—in a piperidine solution of the complex leads to the formation on exposure, not of monoanions, but of a dihydro-derivative which has been observed many times in previous work on the photoreduction of magnesium phthalocyanine[87]. Nevertheless, there are no grounds for doubting that monoanions are formed at the initial stage even in this case, subsequently add a proton, and pass through a stage of disproportionation with conversion into the dihydro-derivative.

N-Methylpiperidine in dimethylformamide can also be used as reductant for the photochemical production of singly charged anions of magnesium phthalocyanine. In this system illumination with visible light at $-60°C$ gives initially monoanions, then a dihydro-derivative with an absorption band at 560 nm, and finally a new product with a band at 780 nm.[26] This latter spectrum was identical with that of a protonated form of tetra-anions of the complex[21], and the product was probably a tetrahydro-derivative.

Monoanions of several other metal phthalocyanines can be obtained in dimethylformamide with hydrazine or *N*-methylpiperidine as reducing agent[26]. Those of the lead and cadmium complexes obtained in this way were spectroscopically indistinguishable from singly charged phthalocyanine anions. These compounds probably lose their metal atoms immediately after addition of an electron: i.e. a phenomenon takes place analogous to the photophaeophytinisation of chlorophyll on reduction[92]. Copper and nickel phthalocyanines on exposure form monoanions with the typical absorption spectrum characteristic of localisation of the added electron on the ligand. Cobalt phthalocyanine is reduced to a monoanion with localisation of the charge on the cobalt atom. In the presence of *N*-methylpiperidine in dimethylformamide alone or in an equimolecular mixture with oxolan at $-60°C$ iron phthalocyanine is reduced photochemically to monoanions having an absorption spectrum indicating a distribution of charge between the ligand and the iron atom, as in

the reduction of the metal complex by an alkali metal. Cooling a solution of monoanions of iron phthalocyanine to −196°C changes the spectrum, and the charge shifts to the ligand (thermochromism—see above).

Application of this method for the photogeneration of ions in liquid solutions to tetraphenylporphin and its zinc derivative [67,93] also yielded monoanions at −60°C, although their yield was only 60%. This may have been due to the photoinduced reverse reaction. When heated to 20°C these monoanions are converted partly into a dihydro-derivative and partly into the original compound. Protonation was not observed with ions of phthalocyanine and metal phthalocyanines, probably owing to their greater stability towards protonation.

The ionic character and the magnitude of the charges on the products of the above photoprocesses have been confirmed by e.s.r. measurements [91] and by photoelimination of an electron leading to regeneration of neutral molecules of the original tetrapyrrole compound (or its monoanion if the electron has been detached from the dianion) [43,67].

Sufficient data are not yet available to settle the mechanism of the photogeneration of molecular ions, and only certain general considerations can be expressed. The act of electron transfer occurs between a photoexcited molecule of the tetrapyrrole compound Por* and an electron-donating molecule Don:

$$Por^* + Don \rightarrow Por^- + Don^+ .$$

The electron donor may be either a solvent molecule (as occurred in the reduction of magnesium phthalocyanine by piperidine) or an added reactant molecule (hydrazine in dimethylformamide); these cases may differ significantly in reaction kinetics. The excited molecule Por* is most often present in the lowest triplet state, but activity in the charge transfer may be exhibited both by a singlet state and by excited states due to the presence of the d-shell of the central metal atom [94]. A special case is the photogeneration of iron phthalocyanine monoanions and also of dianions of phthalocyanine and the magnesium complex. These reactions do not occur on exposure in the region of long-wavelength absorption bands but require short-wavelength bands, which suggests that higher excited states are involved in these photoreactions. Since the lifetimes of such states are usually brief, diffusion processes must play an insignificant part, and the electron donors must be either solvent molecules from the solvate sheath or out-of-plane added molecules present in a complex with the Por* molecule.

The stability of photogenerated negative ions of tetrapyrrole compounds in liquid solutions is determined firstly by the solvating properties of the solvent and secondly by the ability of the positive gegenions Don^+ formed in the photoreaction to be deactivated in time to prevent electron transfer in the opposite direction. The actual occurrence of such deactivation is confirmed by the absence from the e.s.r. spectra of signals due to radical-cations. The most probable mechanism of deactivation is interaction with solvent molecules or with neutral molecules of the donor.

In solid solutions (predominantly solutions frozen at −196°C, but polymerised matrices can in principle be used) the general mechanism of the phototransfer of an electron is the same as in liquid solutions, but conditions for stabilisation of the ions differ considerably. Molecular diffusion is slowed down, and the presence of proton-donating and electron-accepting impurities does not affect the stability of negative ions provided that these impurities do not form complexes with molecules of the tetrapyrrole compound and do not enter their solvate sheaths.

Krasnovskii and his coworkers [95] reported the possibility of the photochemical generation and stabilisation of radical-ion forms of porphin in acidified alcoholic solutions at −196°C. Gribova detected radical-ions on irradiating frozen alcoholic solutions of magnesium aetioporphyrin [96]. The hypothesis that these radical-ions were monoanions of the complex was not supported by later work: exposure of frozen solutions of zinc and magnesium aetioporphyrins in mixtures of diethyl ether with ethanol or with oxolan results in detachment of an electron from the molecules of these compounds and formation of their monocations. Negative ions may also be formed in subsequent stages of the reaction as a result of migration of the freed electrons [97,98]. Magnesium phthalocyanine, in contrast to magnesium aetioporphyrin, is converted into monoanions on exposure in a frozen ethereal oxolan matrix [90]. The porphyrin ring is obviously a better electron donor than is the phthalocyanine ring. Monoanions of zinc tetraphenylporphin may be photogenerated in frozen pyridine, and were recorded in photoconductivity experiments [99].

An interesting case of electron phototransfer from negative pyridine ions to zinc aetioporphyrin molecules has been observed in a frozen mixture of oxolan and ether [75]. When solutions of these species are mixed, they form a complex which in the frozen state is highly photosensitive: brief exposure in any of the absorption bands of zinc aetioporphyrin converts it into monoanions, which with increase in exposure eliminate the extra electron and regenerate the neutral molecule. Magnesium, copper, nickel, and disodium aetioporphyrins do not form complexes with pyridine ions under similar conditions, and in frozen solutions possess no photosensitivity to visible light. Thus slight individual peculiarities of different tetrapyrrole compounds may be efficacious under certain conditions.

In acid medium two protons add to a molecule of a metal-free porphyrin, with formation of a porphyrin dication [100]. The presence of the positive charge enhances its electron affinity: the acid dicationic form of a porphyrin can be reduced not only in the presence of typical reducing agents but even by anions of mineral acids. Photochemical reduction of the acid cationic forms in frozen solutions may yield either ionic or hydrogenated forms. The photoprocesses can be directed towards either reduction or oxidation by varying the composition of the incident radiation by introducing typical oxidants or reductants into the solution [25,101,102].

Frozen solutions enable molecular ions to be generated by γ-radiolysis, which effects electron transfer between solvent and solute molecules. Depending on the properties of the solvent the solute molecules can be converted into either anionic or cationic forms. The advantage of this method is that the resulting ions do not interact with the gegenion. Though widely used for investigating ions of aromatic compounds, γ-radiolysis has hardly been applied at all to the generation of tetrapyrrole ions. Only one paper has been published, on the radiolysis of chlorophyll: irradiation in frozen methyloxolan gave monoanions, and exposure in isobutyl chloride yielded monocations [103].

VI. COMPLEXES. IONIC ASSOCIATION

The formation of molecular complexes (association) is a widespread phenomenon with neutral molecules, and has been investigated in detail. The presence of the excess

charge in a molecular ion, by introducing a specific character into its interaction with the medium, not only does not prevent but rather promotes such interaction. The specific character of a molecular ion governs the association of ions of opposite sign. In solution this phenomenon leads to the formation of ion-pairs (e.g. comprising a molecular anion and an alkali-metal cation) or larger aggregates. In the solid state ionic association leads to the formation of saltlike products. Another feature of interaction of a molecular ion with the medium is its enhanced capacity for solvation in solution. The excess charge of the ion ensures a more stable orientation of the molecular dipoles surrounding it and deeper potential wells formed by the solvating dipoles. This ability of ions to form stable solvates makes it possible to stabilise the ions in liquid solutions.

Furthermore, molecular ions can also be involved in the interactions usually observed between neutral molecules. For example, monocations of perylene and tetracene form dimers by donor–acceptor interaction [104]. We have discussed above complexes comprising a negative ion and a neutral molecule, which are probably weak charge-transfer complexes in which the negative ion obviously acts as electron donor. Such are the complexes between the iron phthalocyanine monoanion and a neutral molecule of an organic base, whose formation leads to a redistribution of charge in the monoanion, and the complex between a negative ion of pyridine and a neutral molecule of zinc aetioporphyrin. The latter complex is not formed if the component solutions are mixed and kept at or below −100°C: complex formation takes place only around −60°C. The need to raise the temperature for complex formation to occur is obviously due to the necessity of rearrangement of the solvate sheaths surrounding the pyridine ions and the zinc aetioporphyrin molecules. The sheath around the pyridine ions, which bear an excess negative charge and therefore exert an enhanced orienting effect on the surrounding dipoles, exhibits especially great stability, which increases the lower the temperature. Once the complex has been formed at −60°C, of course, it does not decompose when the temperature is subsequently lowered [75]. Exposure entails electron transfer within the complex, with formation of the zinc aetioporphyrin monoanion—not dianions—so that the complex must be regarded as equimolecular.

Returning to the phenomenon of ionic association, we note that in general an equilibrium is established in solution between ion-pairs of various types (contact, separated) and dissociated ions [1-3,9,105]. The solvating properties of the solvent become stronger with fall in temperature, and the equilibrium shifts towards separated and dissociated ion-pairs. The position of equilibrium depends on the solvating power of the solvent, the dimensions of anion and cation, and the charge on the molecular ion: a multicharged ion retains gegenions more firmly than does a singly charged ion. In methyloxolan, in particular, the monolithium salts of anthracene, tetracene, and pentacene, both at 20 and especially at −196°C, are dissociated or form separated ion-pairs differing little in properties from dissociated ions. Monosodium and monopotassium salts of polyacenes exist in this solvent at 20°C predominantly as contact ion-pairs, which are converted into separated pairs or dissociated ions when the temperature is lowered. Dianions of polyacenes are associated with two positive ions at 20°C, but in most cases with one such ion at −196°C. [3,106,107]

No detailed investigations have been made on the association of negative ions of tetrapyrrole compounds. Preliminary data show that they obey the same laws as do the ions of aromatic compounds. Although it was suggested that ionic association was strengthened by lowering the temperature of solutions of singly charged magnesium phthalocyanine anions, the grounds for such a hypothesis were insufficient [21], and it must be abandoned in the light of later results. As in the general case, lowering the temperature of solutions of metal phthalocyanine anions probably displaces the equilibrium towards the dissociation of ion-pairs.

Comparison of the absorption spectra of negative ions of metal phthalocyanines at 20°C and at −196°C shows that in an ether–oxolan mixture all ions—from monoanions to tetra-anions—change their state of association with change in temperature. An exception is the cobalt phthalocyanine monoanion, in whose spectrum no change was observed over the above temperature range. An explanation of the absence of change is that the absorption bands of this anion are due to transitions between energy levels of a ligand not bearing a negative charge that, on interaction with the positive charge of a cation, might cause a displacement of levels and bands as occurs with anions of other metal phthalocyanines [44]. The absence of spectral changes with variation in temperature does not mean, of course, that the equilibrium between aggregates and dissociated ions does not shift.

Since an obvious difference is observed [21,44] between the absorption spectra of solutions of metal phthalocyanines at 20°C and at −196°C, it must be supposed that in the former case they are associated with alkali-metal cations, but in the latter case are present as separated ion-pairs or in a dissociated state. The state of association of monoanions of other tetrapyrrole compounds—zinc tetraphenylporphin [20,93], zinc aetioporphyrin [26], disodium chlorin [32]—changes similarly when the temperature is lowered.

On the basis of available experimental data it is difficult to say anything definite on the state of association of multicharged ions of tetrapyrrole compounds, other than that this state changes when the solutions freeze. Comparison with the properties of anions of aromatic compounds suggests that, in oxolan at 20°C, the multicharged ions form aggregates in which the number of alkali-metal cations is equal to the anionic charge. With fall in temperature these aggregates partly dissociate, eliminating one alkali-metal cation—or less probably two cations—as a consequence of the strengthening solvating power of the solvent. It is to be hoped that a detailed study of electron photoelimination from multicharged ions will enable the structure of aggregates in frozen solutions to be refined, since the spectral threshold of such photoelimination should depend significantly on the state of association of the ions: the more complete is dissociation, the more easily can photoelimination be accomplished right up to conversion of the multicharged anion into a neutral molecule.

Electron photoelimination enables ionic aggregates of unusual composition to be obtained in a frozen solution. Thus in methyloxolan at −196°C monoanions of terphenyl and tetracene are usually present in the dissociated state. By detaching an electron from the dianion, which at this temperature is associated with one sodium cation, it was possible to obtain under these conditions associated monoanions clearly distinguishable by their absorption spectra from the dissociated monoanions [107]. Detachment of an electron from magnesium phthalocyanine dianion in a frozen ether–oxolan mixture gave a monoanion with a spectrum similar to that of the monoanion at room temperature [21]. Comparison of this experiment with those on the photodischarge of dianions of terphenyl and tetracene

indicates that the same phenomenon is observed even in this case, i.e. that magnesium phthalocyanine dianion is associated with one sodium cation in frozen solution. The photodetachment of one electron from the dianion gives the associated monoanion, which does not normally exist in frozen solution. Complete photodischarge of the dianion should result in formation of the neutral magnesium phthalocyanine molecule in direct contact with the alkali-metal cation. The photodischarge of tetra-anions may yield a metal phthalocyanine molecule surrounded by two or three cations, which opens up the possibility of investigating the properties of a molecule in the field of contiguous charged species.

VII. CATALYTIC ACTIVITY OF NEGATIVE IONS OF METAL PHTHALOCYANINES

Although molecular ions are involved as intermediate structures in most redox reactions, their use as reactants is still fairly limited. The ability of negative ions to transfer an electron to compounds of greater electron affinity makes possible their use for reductions, including the initiation of anionic polymerisation [108]. Anions of aromatic hydrocarbons, obtained on interaction with alkali metals, can be employed in metallations [109]. Use of the protonation of negative ions to obtain hydrogenated derivatives of the compounds is a promising possibility. It must be supposed that negative ions of tetrapyrrole compounds can be employed in the same reactions as ions of aromatic compounds. The existence of multicharged ions of metal phthalocyanines and the localisation of the negative charge either on the tetrapyrrole ligand or on the complexing metal atom may extend significantly the potential use of ions of metal phthalocyanines and porphyrins as selective reactants. Hitherto, however, hardly any investigations on these lines have been made on ions of tetrapyrrole compounds. Information is available only on a series of Japanese studies in which negative ions of tetrapyrrole compounds, mainly metal phthalocyanines, were used as catalysts.

Neutral metal phthalocyanines catalyse, for example, hydrogen exchange, the conversion of para- into ortho-hydrogen, the oxidation of cumene to its hydroperoxide, and the dehydrogenation and decomposition of formic acid [110,111]. In several cases the catalytic activity is determined by the nature of the central metal atom, but with heterogeneous catalysis the rate of reaction is significantly affected by the crystalline modification of the metal phthalocyanine, which indicates the part played by the π-conjugated system of the tetrapyrrole ligand [110]. Polymeric metal phthalocyanines, which have an extended π-electron system, exhibit catalytic activity towards reactions involving activation of hydrogen atoms that exceeds the activity of the monomeric complexes by an order of magnitude [111].

The negative ions of metal phthalocyanines, which are distinguished from the neutral molecules by a higher π-electron density in the tetrapyrrole ring, exhibit a significantly higher catalytic activity than the latter. In 1966 Ichikawa et al. discovered [112,113] that "donor–acceptor complexes" formed on contact between a sublimed film of a metal phthalocyanine and sodium vapour effectively catalyse hydrogen exchange between molecular hydrogen and deuterium, and between acetylene and deuteroacetylene. These "donor–acceptor complexes" were later identified with ionic salts of the metal phthalocyanines [114,115], and were found to catalyse several other chemical reactions, in particular the hydrogenation of alkenes in isomerisations, the synthesis of ammonia from hydrogen and nitrogen, and that of hydrocarbons from carbon monoxide and hydrogen [114,116,117]. It was found also that two central hydrogen atoms in sodium phthalocyanine were replaced by deuterium in the presence of molecular deuterium or deuteroacetylene. Negative ions of metal phthalocyanines also exchange their hydrogen for deuterium atoms [118,119]. This implies that hydrogen exchange takes place even in the benzene rings of metal phthalocyanine ions [113]. The excess negative charge of the ion, being distributed over the phthalocyanine ring, obviously covers the benzene rings also, whence the latter become more protophilic, which makes possible hydrogen exchange between magnesium phthalocyanine ions and deuterium molecules (or deuteroacetylene). This conclusion is supported directly by the increased rate of isotopic exchange between molecular deuterium and the metal phthalocyanine ion with increase in the ionic charge, but only slight variation with the nature of the central metal atom [115]. Exceptions are the monoanions of cobalt and iron phthalocyanines and the dianion of the latter, which do not exchange their hydrogen atoms for deuterium and catalyse neither exchange in a mixture of hydrogen and deuterium molecules nor the hydrogenation of alkenes by hydrogen [120,121]. The reason for such exceptions becomes clear from the electronic structure of these ions (see above): almost all the excess charge in the complex cobalt monoanion is concentrated on the cobalt atom, and a considerable proportion is localised on the iron atom in the complex iron monoanion. Multicharged ions of cobalt and iron phthalocyanines exhibit catalytic activity, as do the ions of other metal phthalocyanines.

The possibility of isotopic exchange between metal phthalocyanine ions and molecular deuterium of deuteroacetylene opens up a route for obtaining under laboratory conditions completely deuterated metal phthalocyanines, which are necessary for spectroscopic investigations on these compounds.

Whereas isotopic exchange between molecular deuterium and metal phthalocyanine ions is little affected by the nature of the metal atom, the hydrogen exchange between molecular hydrogen and deuterium catalysed by these ions depends significantly on the metal atom. The two reactions obviously have different mechanisms. Dissociative chemisorption of the hydrogen (deuterium) molecule in the vicinity of the central metal atom is assumed to be a stage in the latter reaction [115]. The mechanism of isotopic exchange in the benzene ring is obscure: it may be effected either by direct contact between the ring and a deuterium molecule or by contact with atomic deuterium formed by dissociative chemisorption on a neighbouring metal phthalocyanine ion.

The above series of papers on the catalytic action of negative metal phthalocyanine ions contain insufficient spectroscopic data, without which it is difficult, firstly, to monitor the identity of the ionic forms and their stability during an experiment, and secondly, to compare the results with those of other investigations on such ions made predominantly by spectral methods. An unsuccessful attempt was made to obtain infrared absorption spectra of negative ions of phthalocyanine: the spectrum of the initial phthalocyanine film remained unchanged after contact with sodium vapour. Hence it was concluded that formation of ions and catalysis take place only in the surface layer of the film [118,119]. This seems to us a dubious result, as the colour of metal phthalocyanine films was changed by con-

tact with sodium vapour[119]. Using the same method as the Japanese workers, we obtained without special difficulty the electronic and infrared absorption spectra of various ionic forms of magnesium phthalocyanine after films of the neutral complex had been kept in an alkali-metal vapour[122]. This means that the alkali-metal atoms are able to penetrate inside microcrystals of the metal phthalocyanine. Furthermore, comparatively thick films of a metal phthalocyanine are permeable to such small and even large molecules as water, ammonia, phenylhydrazine, aniline, diphenylamine, pyridine, indole, etc.[123,124] This implies that catalysis can occur not only on the surface of films of metal phthalocyanines and their ionic forms but also inside the layer.

Catalytic activity towards various chemical reactions is not an exceptional property peculiar to ions of metal phthalocyanines, as was to be expected. Such activity has been observed with negative ions of metal tetraphenylporphins[125-127], as well as with negative and positive ions of several other organic compounds—tetracyanopyrene[128], phenothiazine[129], polyacenes, quinones, nitriles, and several other aromatic compounds[114,116,120].

Detailed investigation (kinetic and spectroscopic) of the mechanism of the interaction of negative ions of anthracene with hydrogen showed that the product was an anthracene carbanion (the anion of 9-hydroanthracene)[116,130-132]. Carbanions of anthracene are probably formed also in hydrogen exchanges catalysed by anthracene ions and in the hydrogenation of alkenes. The kinetics of the sorption of hydrogen on metal phthalocyanine ions resembles that of the interaction of hydrogen with anthracene ions, but no changes were detected in the electronic absorption spectrum of a film of nickel phthalocyanine tetra-anions in the presence of molecular hydrogen, which was assumed[115] to exclude the suggested possibility of the formation of protonated anions of nickel phthalocyanine.

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Polymeric Charge-transfer Complexes

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Research results on polymeric donor-acceptor complexes both in the solid state and in solution are summarised. Solid polymeric charge-transfer complexes (crystals, films) are semiconducting materials satisfying the requirements of various branches of science and technology. Study of such complexes in solution reveals several specific features of complex formation in polymer systems and approaches an explanation of the electrophysical characteristics of layers of these complexes in terms of the mechanism of complex formation in solution. A brief account is given of the theory of charge-transfer complexes. Methods for determining and calculating the equilibrium constants of the polymeric complexes are critically examined. A list of 172 references is included.

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I. INTRODUCTION

According to modern ideas charge-transfer complexes are compounds formed by the interaction of two valency-saturated molecules—an electron donor D and an electron acceptor A—the former possessing a filled molecular orbital of quite high energy and a low ionisation potential, while the acceptor has a fairly low vacant molecular orbital and considerable electron affinity[1-7]. The transfer of charge from donor to acceptor forms an intermolecular donor-acceptor bond, probably together with various other types of interaction, including polarisation, dipole-dipole, and also van der Waals forces[8].

The properties and the structure of charge-transfer complexes depend in considerable measure on which donor and acceptor orbitals are involved in forming the intermolecular bond. This principle constituted the basis of Mulliken's classification of these complexes[9], in which he divided all donors into three groups—n, σ, and π— according to a structural criterion. The energetically highest orbital in the first group is a lone pair of n-electrons of a heteroatom (R_2O, R_2S, R_3N, etc.), in the second group the electron pair forming an σ-bond (R-Hal), and in the third group a pair of π-electrons in an unsaturated or an aromatic compound. Acceptors are also divided into three groups—v, σ, and π— containing as lowest molecular orbitals respectively a vacant v-valent orbital of the metal atom (metal halides, certain organometallic compounds), a non-bonding σ-orbital (molecular iodine and bromine, iodine monochloride, etc.), and a system of π-bonds (aromatic and unsaturated compounds containing electron-accepting substituents).

Typical organic acceptors-nitro-derivatives of hydrocarbons, anhydrides and chlorides of di- and poly-carboxylic acids, cyano-derivatives of hydrocarbons, and also quinones and their derivatives—belong mainly to the third group Typical organic donors are present in all three groups in Mulliken's classification.

Combining these types of compounds gives a whole variety of donor-acceptor complexes:

nv ($R_2O \cdot MX_3$)	σv ($RX \cdot MX_3$)	πv ($ArH \cdot MX_3$)
$n\pi$ ($R_2O \cdot ArH$)	$\sigma\sigma$ ($RX \cdot I_2$)	$\pi\sigma$ ($ArH \cdot I_2$)
$n\sigma$ ($R_2O \cdot I_2$)	$\sigma\pi$ ($RX \cdot ArH$)	$\pi\pi$ ($Ar_1H \cdot Ar_2H$) .

At the present time $\pi-\pi$ and $\pi-\sigma$ complexes have been most thoroughly studied, whereas the smallest amount of work has been done on complexes with σ-donors.

Brieglev and Checalla divide charge-transfer complexes into strong and weak[10]: the weaker the donor and acceptor properties of the components, the smaller the gain in energy when they interact, the smaller the fraction of charge transferred, and hence the weaker the complex. The tendency to donor-acceptor interaction increases with decrease in the difference $I_D - E_A$ between the ionisation potential and the electron affinity of the molecules[10]. With very strong donors and acceptors complete transfer of an electron from donor to acceptor is possible in the ground state, with the formation of compounds termed strong complexes or radical-ion salts.

Blyumenfel'd et al. divide charge-transfer complexes into weak and strong on the basis of the decisive role of polar states in the appearance of paramagnetism and current carriers[11]. McConnell's classification of complexes into strong (ionic) and weak (non-ionic) is based on the type of packing of the molecules in crystals[12].

II. THEORY OF CHARGE-TRANSFER COMPLEXES

The most characteristic criterion of the formation of a charge-transfer complex is the appearance of a charge-transfer band, in addition to the absorption bands due to the initial components, in the electronic spectrum. The attempt to explain this band led to the development of several theories of donor-acceptor interaction[14-17], among which Mulliken's quantum-mechanical theory[1,13,18-22], which he developed for weak charge-transfer complexes, is now generally accepted. In this theory the ground state of an equimolecular charge-transfer complex is described by a wave function ψ_N, which can be represented approximately by a linear combination of two functions:

$$\Psi_N = a\Psi_0(D, A) + b\Psi_1(D^+ - A^-) \quad (1)$$

where ψ_0 is the wave function corresponding to the structure of the complex with van der Waals interaction (the wave

function of the non-bonded state), and ψ_1 is the wave function of the dative (bonded) state. With weak complexes $a \gg b$, and with strong complexes $b > a$. The lowest excited state of the complex is described by the wave function ψ_E, also a linear combination of wave functions ψ_1 and ψ_0 corresponding to the ionic and neutral states:

$$\Psi_E = a^*\Psi_1(D^+ - A^-) - b^*\Psi_0(D, A) \,. \qquad (2)$$

For weak complexes $a^* \simeq a$ and $b^* \simeq b$. Transition of the complex from the ground to an excited state is responsible for the appearance of the additional band in its absorption spectrum. The energy of such a transition is

$$E_{chtr} = h\nu_{chtr} = W_E - W_N \,. \qquad (3)$$

Fig. 1 gives a diagram of the energy transitions for weak charge-transfer complexes[30].

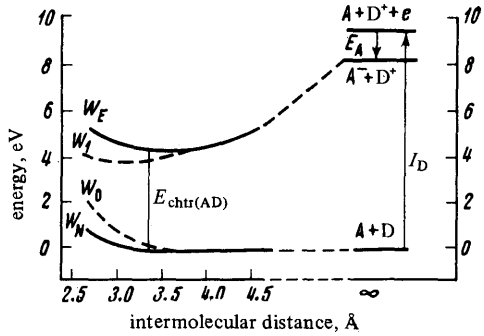


Figure 1. Energy relations of weak charge-transfer complexes between a donor D and an acceptor A, where W_N is the energy corresponding to the ground state of the wave function $\psi_{N(AD)}$ and W_E is the energy corresponding to an excited state of the wave function $\psi_{E(AD)}$, with W_0 and W_1 the corresponding energies in the absence of resonance stabilisation, and $E_{chtr(AD)}$ the energy of the optical intermolecular transition with transfer of charge[22].

The quantum-mechanical expression for the charge-transfer energy is

$$E_{chtr} = h\nu_{chtr} = \frac{(W_1 - W_0)}{(1 - S_{01}^2)}\left[1 + \frac{4\beta_0\beta_1}{(W_1 - W_0)^2}\right]^{1/2} \qquad (4)$$

where W_1 and W_0 are the energies of the dative and non-bonded structures,

$$S_{01} \equiv \int \Psi_0\Psi_1 d\tau$$

is an overlap integral, and

$$\beta_0 = (H_{01} - S_{01}W_0), \quad \beta_1 = (H_{01} - S_{01}W_1), \quad H_{01} = \int \Psi_0 H \Psi_1 d\tau,$$

where H is the Hamiltonian for the whole system of nuclei and electrons. Mulliken showed that, for interaction to occur between the structures ψ_0 and ψ_1, both S_{01} and H_{01} should differ from zero, which means that, in all cases other than strong spin–orbital coupling, the functions ψ_0 and ψ_1 have the same spin. He confirmed by quantum-mechanical calculations that electron transfer takes place with retention of spin.

Phenomenological examination of the transfer of charge leads to the formula

$$h\nu_{chtr} = I_D - E_A - \frac{e^2}{R_{D^+,A^-}} \qquad (5)$$

where I_D is the ionisation potential of the donor, E_A the electron affinity of the acceptor, and $e^2/R_{D+,A-}$ the Coulombic attraction.

Many empirical equations for the energy of charge transfer in complexes of different donors with a particular acceptor have the general form[23]

$$h\nu_{chtr} = cI_D - e_A \qquad (6)$$

where c and e_A are constants.

Further advances in the theory of charge-transfer complexes entail the description of the energy of complex formation by the method of molecular orbitals[24] and also the application of the free-electron model to these complexes[25].

III. CHARGE-TRANSFER COMPLEXES BASED ON POLYMERS AND THEIR ELECTROPHYSICAL PROPERTIES

Numerous research results on the properties of donors and acceptors, conditions for the preparation of pure charge-transfer complexes, and their structure, stability, and role in organic reactions and biochemical processes have been summarised in monographs[1–5,26]. Special mention need be made only of work during recent years on the use of such complexes as initiators in the polymerisation of monomers exhibiting donor properties, e.g. *N*-vinylcarbazole[27–36] and propylene sulphide methylthi-iran[37].

Special attention has been paid to investigating the semiconductor properties of charge-transfer complexes[38–42]. The complexes exhibit exhanced electrical conductivity[43–46], the activation energy of which (1.5–0 eV) varies linearly with the energy of charge-transfer[45–47]. The theoretical and practical interest in new highly conducting materials has recently stimulated a great development of work on charge-transfer complexes based on polymers. The principle of introducing a polymeric molecule into the complex has been used for example, to prepare a series of chelate compounds, with polymeric phthalocyanine[48], polypyromellitimide[49], and polymeric tetracyanoethylene[50] as ligands. Interest in polymeric complexes is connected with the possibility of improving the conductance by increased intermolecular interaction on complex formation by chain molecules[51] and with use of the film-forming properties of polymers in semiconductor technology.

All the polymeric donors studied can conveniently be classified according to the structure of the repeating unit: (I) polystyrene and its derivatives; (II) polymers with aromatic ring systems in a side-chain; (III) polymers with a heteroatom (usually a nitrogen atom) in a side-chain; and (IV) polymers having a conjugated system in the main chain (Table 1). The acceptors usually studied have been benzoquinone derivatives (chloranil, bromanil, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, and 7,7,8,8-tetracyanoquinodimethane), 1,3,5-trinitrobenzene, silver perchlorate, molecular bromine and iodine, and tetracyanoethylene.

All the complexes (Table 1) exhibit an exponential temperature dependence of electrical conductivity:

$$\sigma = \sigma_0 \cdot \exp(-\epsilon/kT) \qquad (7)$$

where ϵ is the activation energy, which has values of 0.8–0 and 1.5–0.01 eV according to Knoesel[52] and Paushkin[53] respectively. The corresponding conductivity ranges are

5×10^{-2}–3×10^{-14} [52] and 10^{-2}–10^{-15} [53] $ohm^{-1}\ cm^{-1}$. Radical-ion salts of tetracyanoquinodimethane possess the highest conductivity[69,74], as also charge-transfer complexes based on polymers having a conjugated system[69,75–79,83]. In most cases a parallelism is observed between the electrical and magnetic properties of charge-transfer complexes having the character of radical-ion salts.

Table 1. Charge-transfer complexes based on polymeric donors.

Polymeric donor	Acceptor	Ref.
	Group I	
Polystyrene	tetracyanoethylene	54, 55
Polystyrene	chloranil	54
Polystyrene	2,3-dichloro-5,6-dicyano-1,4-benzoquinone	54
Polystyrene	silver perchlorate	54
Polystyrene	iodine, bromine	56
Poly-*p*-dimethylaminostyrene	chloranil, bromanil	57, 58–60
Poly-*p*-dimethylaminostyrene	7,7,8,8-tetracyanoquinodimethane	61–63
Polyvinyltoluene	iodine, bromine	56
Styrene–α-methylstyrene copolymer	iodine, bromine	56
Styrene–2-vinylnaphthalene copolymer	iodine, bromine	56
Polyvinylmesitylene	tetracyanoethylene, chloranil, dichlorodicyano-*p*-benzoquinone	54
	Group II	
Polyvinylnaphthalene (atactic)	tetracyanoethylene, chloranil	54, 65
Polyvinylnaphthalene (atactic)	dichlorodicyano-*p*-benzoquinone	54
Polyvinylnaphthalene (atactic)	tetracyanoquinodimethane	63
Polyvinylnaphthalene (atactic)	1,3,5-trinitrobenzene	65
Polyvinylnaphthalene (isotactic)	chloranil	54
Polyvinylanthracene	trinitrobenzene, iodine, bromine	66
Polyacenaphthylene	tetracyanoethylene, chloranil	54, 67
Poly-2-vinylnaphthalene	tetracyanoquinodimethane	62
Poly-2-vinylnaphthalene	various	62
	Group III	
Poly-4-vinylpyridine	various	69
Poly-4-vinylpyridine	tetracyanoquinodimethane, antimony pentachloride	70, 64
Poly-4-vinylpyridine	iodine	68
Poly-4-vinylpyridine	chloranil, iodine, tetracyanoquinodimethane	74
Poly-2-vinylpyridine (atactic)		
Poly-2-vinylpyridine (isotactic)	tetracyanoquinodimethane	74, 63
Poly-*N*-vinylcarbazole	tetracyanoquinodimethane	71
Poly-*N*-vinylcarbazole	antimony trichloride, iodine	72
Poly-*N*-vinylcarbazole	iodine	73
Poly-*N*-vinylcarbazole	tetracyanoethylene, chloranil, trinitrobenzene	65
	Group IV	
Polydiphenylamine	tetracyanoethylene, chloranil, iodine	75
Polymeric Schiff bases	iodine, bromine	76
Polyphenylenes	iodine	77
Polyethynylnaphthalene	tetracyanoquinodimethane, iodine	78
Radiation-thermal polyethylene	iodine	81
Polyphenylacetylene	iodine	80
Polyethynylpyridine	tetracyanoquinodimethane	69

Studies have been made not only on the systems listed in Table 1 but also on charge-transfer complexes from polymers obtained by polycondensation, polymers containing ferrocene (with iodine, picric acid, and tetracyanoethylene as acceptors)[82], polyesters of aryliminodiethanols (with tetracyanoethylene, chloranil, and dichlorodicyano-*p*-benzoquinone)[83], and albumen (with chloranil)[84]. Systems have also been examined in which the polymer was an electron acceptor, while a compound of low molecular weight served as donor[85], e.g. complexes of poly-2,4-dinitrostyrene with amines[55]. Stable charge-transfer complexes possessing semiconductor properties have been reported[86] from the copolymerisation of monomers having strongly electron-accepting groups (trinitrostyrene) and electron-donating groups (4-vinylpyridine, *p*-dimethylaminostyrene). Among the most interesting polymers are polyphenylenaminochloranils, which contain both electron-donating and electron-accepting groups in the macromolecular chain[87].

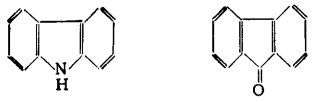
Highly photoconducting systems are of the greatest interest among polymeric semiconductors[88]. Although all insulators and semiconductors are photosensitive, the number of substances suitable for practical use as photosemiconductors is extremely limited. The reason is that many factors governing the photosensitivity of a substance depend on defects in its crystal structure, and only in certain materials and structures is the nature of these defects such that the excited current carriers are sufficiently long lived[88]. Polymers, in particular, are characterised by an immense number of defects in the solid state (regions of differing orientations of crystallites, irregularities in the packing of sheets and strips, etc.). The photosensitivity of many polymers has been studied, including polyconjugated polymers[83], biopolymers[89], polystyrene[90], and polyvinylcarbazole[91]. The mechanism of photoconduction in polymers probably involved as first step excitation of the macromolecule by an absorbed photon, followed by migration of the excited state (exciton) until it encounters a structural or chemical defect, on which a free pair of photocurrent carriers is formed[92].

Polyvinylcarbazole obtained in the presence of a Lewis acid as initiator is more strongly photosensitive than is the thermal polymer[91]. Thus the photosensitivity of the polymer is sensitised by the formation of a charge-transfer complex between the acceptor (the Lewis acid) and the electron donor (the polymer). It has been reported that various chemical compounds sensitise several polymers[91], in particular polyacenaphthylene[93], polyvinylpyridine[74], polystyrene[90], polydiphenylbutadiyne[94], β-iodophenylacetylene[95], and polyvinylcarbazole, which has been the most thoroughly studied during recent years[96–100]. This last polymer possesses thermoplasticity, forms photosensitive, transparent films, and currently finds practical application in electrophotography[91,101–105] (this process consists in producing an electrostatic image in the photosensitive memory layers and then developing it with dyes[106–108]).

A fundamental aspect of the study of the functioning of polymeric charge-transfer complexes under electrographic conditions is to ascertain the mechanisms of complex formation and of photoconduction. Weigle, for example, considers that, on excitation with a light quantum, the complexes inject holes into the valency band of the polymer, whose chains become conducting[109]. Hoegl discusses the mechanism of photoconduction in terms of the types of donor and acceptor[91]. However, the plethora of polymer systems has hitherto prevented the development of a unified view on the mechanism of photoconduction. An important problem is to establish a correlation between the photoconductance and the physicochemical properties of the components of the electrographic layer as well as its structure. Many authors relate the photoconductance to the electronic properties of the acceptor. Thus Meier and Albrecht[110] studied the effect of electron acceptors on the photosensitivity of thin *p*-type merocyanine and phthalocyanine films, and found only a rough correlation between the electron affinity of an acceptor and its ability to sensitise photoconduction. Smith and Weigle[111] tried to correlate spectral photosensitivity with the electron affinity of the acceptor. They conclude in a series of papers that the photosensitivity and the stability of charge-transfer complexes are influenced not so much by the electron affinity as by the spatial dimensions of the components. Thus the complexes of two similar π-systems are more stable than those formed by a donor and an acceptor differing in size[112]. Pyrene forms stronger complexes with tetracyanoquinodimethane than with tetracyanoethylene (K = 78.4 and 29.5 M^{-1}). Hayashi et al. found that the sensitising power of acceptors of the series

—*p*-benzoquinone, 1,4-naphthaquinone, 9,10-anthraquinone—diminishes with increase in their electron affinity[97]. Since these acceptors differ comparatively little in electron affinity (0.5, 0.7, and 0.77 respectively), the size of the π-system is an important factor in their sensitising power. This may be an indication that the stability constant of the complex is a more important parameter in the choice of an effective additive for a given electron-donating photoconductor than is the electron affinity of the acceptor.

Interesting results were obtained by Wagner and Gasner[113], who studied the photosensitivity of polyvinylcarbazole with several acceptors, including nitro-derivatives of fluorenone, an important feature of whose structure (II) is its similarity to that of carbazole (I):



(I) (II)

All the fluorenone derivatives, while differing in electron affinity, fitted on a straight line when the rate constant of the decay of the photocurrent was plotted against electron affinity, whereas points departing from the correlation, and enclosed by the full line in Fig. 2, correspond to acceptors differing in molecular size of the carbazole unit. Thus the photoconductance correlates with the electronic properties of the acceptor only in a homologous series of acceptors with the steric factors of the components taken into account. No correlation is found[114] between the thermodynamic characteristics of charge-transfer complexes of polyvinylcarbazole and of polystyrene with various acceptors and the photoelectric sensitivity under electrographic conditions.

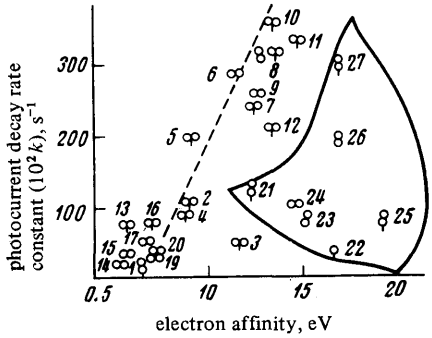


Figure 2. Dependence of photocurrent decay rate constant in charge-transfer complexes of polyvinylcarbazole on electron affinity of a series of acceptors[113]: *1*)–*20*) nitrofluorenone derivatives; *21*) 3,3′,5,5′-tetramethyldiphenoquinone; *22*) *o*-chloranil; *23*) *p*-chloranil; *24*) 2-dicyanomethylenindane-1,3-dione; *25*) 2,3-dichloro-5,6-dicyano-1,4-benzoquinone; *26*) tetracyanoethylene; *27*) 7,7,8,8-tetracyanoquinodimethane.

Recently investigators have increasingly arrived at the conclusion that the photosensitivity of a layer should be influenced by its physical macrostructure. Kryszevski, for example, regards all structural defects as traps within a forbidden energy band[115,116]. Electron microscopy has shown the appearance of supermolecular structures of dendritic type in films of charge-transfer complexes based on poly(phenyl methacrylate), poly-(2-naphthyl methacrylate)[117], polyvinylcarbazole, and polystyrene[118]. Such dendritic structures are absent from films of pure polymers. The formation of supermolecular structures is attributed to the increase in chain rigidity of polymeric charge-transfer complexes during complex formation in solution.

IV. PHYSICAL CHEMISTRY OF POLYMERIC CHARGE-TRANSFER COMPLEXES IN SOLUTION

The technology of the production of electrographic layers based on polymeric charge-transfer complexes involves solutions of polymers, so that a study of molecular aspects of the formation of such complexes in solution followed by interpolation of the results into the solid complexes is of great theoretical and practical value. A fair number of publications on the chemistry of polymeric charge-transfer complexes in solution have appeared recently.

In a study of the formation of complexes by poly-2-vinylpyridine and by its styrene copolymer with halide ions in 0.5*N* sulphuric acid Slough[119] noted that both π- and n-charge transfer is possible in heteroaromatic systems, so that they yield stronger complexes than do purely aromatic systems. The intensity of the charge-transfer band at 280–400 nm increased in the sequence—chloride < bromide < iodide—in parallel with the polarisability of the halide ions. The differing force of interaction of ions with a polymer can be used for the production of selectively anion-permeable membranes[120].

Klöpffer and Willicks[121] made a broad spectroscopic investigation of complexes formed by several polymeric donors and by their low-molecular weight analogues with various electron acceptors. Complexes of tetracyanoethylene with poly-10-methyl-3-vinylphenothiazine and with *N*-methylphenothiazine have a double absorption band in the region of 9600 cm^{-1}, which they attribute to splitting of the energy level of the donor in the ground state, so that two ionisation potentials are observed. The complex of poly-*p*-dimethylaminostyrene with tetracyanoquinodimethane exhibits in solution a double band in the range 11 750–13 200 cm^{-1}, which is assigned to the radical-anion of the acceptor. Absorption bands in the range 25 000–23 800 cm^{-1} for the complex formed by the same polymer with tetracyanoethylene indicate the formation of a pentacyanopropanide anion, a conversion product of the radical-ion of tetracyanoethylene. The band in the region of 25 600 cm^{-1} in the spectrum of the complex of this polymer with dichlorodicyano-*p*-benzoquinone is also ascribed to absorption by the radical-anion of the acceptor. The stability of the complexes is not always determined by the difference $I_D - E_A$: thus the ionisation potential of poly-10-methyl-3-vinylphenothiazine (7.0 eV), which forms only a weak complex with tetracyanoethylene, is lower than that of poly-*p*-dimethylaminostyrene (7.2 eV), which gives a strong radical-ion complex with the same acceptor. This is probably due to a difference between the energies of polarisation of individual states.

In a study of radical-ion salts Japanese investigators found[70,74] that tetracyanoquinodimethane (TCQDM) forms with polyvinylpyridines two types of complexes—simple $H^+(TCQDM)_2^-$ and double $BH^+(TCQDM)_2^-$.—where B is the radical of the organic base. The absence from the ultraviolet spectra of the absorption band due to the neutral acceptor indicates that the molecule and the radical-anion of the

acceptor form an intermolecular bond in the double complex and add to the same unit in the polymer. The ratio $\epsilon_{\lambda 842}/\epsilon_{\lambda 395}$, where $\epsilon_{\lambda 842}$ and $\epsilon_{\lambda 395}$ are the extinction coefficients of the radical-anion and of the molecule respectively, shows that only every fourth unit of the polymer forms the double complex. When the complexes are kept in the air, $\epsilon_{\lambda 395}$ decreases, while the ratio increases, which corresponds to conversion of the double into the simple complex[70].

In a spectrophotometric study of complexes of poly-*p*-dimethylaminostyrene with chloranil Knoesel[58] observed that in freshly prepared solutions the charge-transfer bands for complexes of this polymer and of its low-molecular analogue coincide, but after some time the band due to the polymeric complex shifts to the red range. This was explained by compaction of the packing of the acceptor between donor groups of the polymer, a phenomenon on which the authors termed "the polymer effect". The displacement of the charge-transfer band of this polymer with chloranil and also with dichlorodicyano-*p*-benzoquinone was confirmed by Klöpffer[121].

Hallensleben isolated[122] and studied[123] complexes of poly-4-vinylpyridine with tetracyanoethylene in solution in methanol and in chlorinated hydrocarbons. The variation in the ultraviolet spectra of the complexes correlated with the time variation of the viscosity. At low polymer concentrations the viscosity tended to constant values, and at high concentrations passed through a maximum. The extinction coefficients of solutions of the complex increased to a constant value. The experimental results were explained by conformational changes in the macromolecular chain on interaction with the acceptor.

Zwick's spectrophotometric study of complexes of polyvinyl alcohol with iodine in the presence of boric acid is distinguished by its elegance and completeness[124]. He showed that the position of the principal absorption maximum of the complex in the range 580–700 nm depends on the relative concentrations of iodine ions, boric acid, and polymer, as well as on the temperature, which is all evidence of the complexity of the process. In the presence of boric acid the polyvinyl alcohol molecule emerges from the coiled conformation and forms helices, which associate and finally crystallise, during which process the channels within the helices of the polymer molecule fill with polyiodide chains and become longer and more regular, all these changes being accompanied by a characteristic blue coloration. A limiting intensity of colour is reached when one iodine molecule is associated with 24 monomer units (two turns of the helix) in the polyvinyl alcohol macromolecule.

The thermodynamics of complex formation in polymer systems was not considered in the work discussed above, although the thermodynamic properties of the lower-molecular-weight charge-transfer complexes have been studied very carefully[1–6]. The most important thermodynamic characteristic of complex compounds in general and of macromolecular compounds in particular is the equilibrium (instability, stability) constant, which is a measure of the free energy of complex formation, although the reliability of this parameter is disputed in several cases (Ref. 5, p.383).

Equilibrium constants of polymeric charge-transfer complexes (formed by iodine with polystyrene and with rubber) were first determined by Evans by the Benesi-Hildebrand method[126], earlier used for low-molecular-weight complexes. According to Evans equilibrium constants and extinction coefficients have the same values for polymers as for model compounds (ethylbenzene, propylbenzene, *cis*- and *trans*-butenes) owing to the isolation of the electron-donor groups in the polymer and the absence of additional steric hindrance in the polymer complexes.

Kryszewski[127] obtained different equilibrium constants for complexes of polymers and of their low-molecular analogues with silver perchlorate. The equilibrium constants for charge-tranfer complexes of atactic and isotactic polystyrene and poly-α-methylstyrene with iodine are respectively 0.14, 0.18, and 0.26 M^{-1}; those for toluene, benzene, styrene, and ethylbenzene agree well with Evan's results[126] and are respectively 0.16, 0.14, 0.15, and 0.17 M^{-1}. It is assumed that complexes of various configurations are formed in solution, the least symmetrical of which is unstable. Therefore complexes based on low-molecular analogues and atactic polystyrene possess the lowest equilibrium constants. In conformity with the theory of contact charge-transfer[128] lower intensities of absorption correspond to higher stability constants:

$$K_{\text{pst,atact}} < K_{\text{pst,isotact}} < K_{\text{pamst}} \cong \epsilon_{\text{pst,atact}} > \epsilon_{\text{pst,isotact}} > \epsilon_{\text{pamst}} .$$

It was shown spectrophotometrically that charge-transfer complexes of *p*-benzoquinone with nitrogen-containing monomers, such as poly-2- and 4-vinylpyridines, poly-2-methyl-5-vinylpyridine, and poly-*NN*-dimethylmethacrylamide, are more stable than the corresponding complexes of their model compounds[120]. However, Markova[69] found from kinetic data that the equilibrium constant for the complex of poly-4-vinylpyridine with tetracyanoethylene is rather smaller than that for 4-ethylpyridine (0.5 and 0.6 M^{-1}). Rembaum et al. studied the charge-transfer complexes of *N*-ethylcarbazole and poly-*N*-vinylcarbazole with tetracyanoethylene in dichloromethane (K = 5.83 and 1.3 M^{-1}), and attributed the lower equilibrium constant for the polymeric complex to steric hindrance in the polymer chain[130]. A similar explanation is given for the complexes of polystyrene and polyvinylcarbazole with quinonoid acceptors, which have smaller equilibrium constants than those of the complexes of model analogues—ethylbenzene, cumene, *N*-isopropylcarbazole[131].

Smets et al. studied complexes formed by polyvinylcarbazole, poly-2-vinylnaphthalene, poly-2-naphthylmethylene, and their simple analogues with several organic acceptors[65]. The equilibrium constants were always smaller for the polymeric complexes than for the model compounds. This relation was preserved even when the constants were determined by nuclear magnetic resonance[132].

An original approach to polymeric donor-acceptor complexes was adopted by Braun and Sterzel[133], who studied the formation of donor-acceptor complexes of a styrene-*p*-dimethylaminostyrene copolymer with chloranil and with dichlorodicyano-*p*-benzoquinone, and found the equilibrium constants calculated by the Benesi–Hildebrand method to be functions of the copolymer composition, the highest values being observed for the complex of the copolymer containing 80 mole % of *p*-dimethylaminostyrene (Fig. 3). From these results it was concluded that the thermodynamic parameters (equilibrium constant $\overline{K}$ and free energy of formation of the complex ΔG) are significantly affected by solvation of donor, acceptor, and complex. On complex formation the mobility of the polymer chain diminishes, the entropy decreases, and hence the absolute value of ΔG increases. The equilibrium constants for the complexes with dichlorodicyano-*p*-benzoquinone exceed those for the chloranil complexes by factors of 10^4–10^5, which is attributed to the difference in electron affinity between these acceptors (1.95 and 1.37 eV respectively).

Iwatsuki and Arai[134] used complexes of the same copolymer with several acceptors (chloranil, trinitrotoluene, iodine, maleic anhydride) to elucidate the "polymer effect".

They observed a bathochromic shift in the charge-transfer band maximum and an increase in the equilibrium constant with lengthening of the continuous sequence of *p*-dimethylaminostyrene units and increase in their mole fraction in the copolymer (Fig. 4). The bathochromic shift was attributed to a fall in the ionisation potential *I* of the polymeric donor resulting from $\pi-\pi$ interaction of the dimethylaniline groups with the phenyl rings. The two-stage character of the variation in equilibrium constant was ascribed to the contribution by the energy of Brownian movement of the polymer chain of the donor to the total free energy of complex formation.

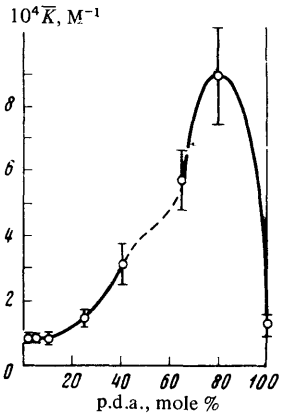


Figure 3. Dependence of equilibrium constant $\bar{K}$ on *p*-dimethylaminostyrene (p.d.a.) content of its styrene copolymer with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone as acceptor and cyclohexanone as solvent[133].

The influence of conformational changes in the macromolecular chains on complex formation has been examined[114,135]. Complexes formed by polystyrene, poly-α-methylstyrene, and polyvinylcarbazole of various molecular weights with several quinonoid acceptors and with tetracyanoethylene showed that the temperature dependence of the equilibrium constant depends on the molecular weight of the polymeric donor. With polymers of comparatively low molecular weight (e.g. polyvinylcarbazole having $\bar{M}_n$ = 1000) the equilibrium constants of the complexes decrease with rise in temperature, as with simple charge-transfer complexes. Complexes of polymers of intermediate molecular weight (polyvinylcarbazole with $\bar{M}_n$ = 30 000) the constants vary very little with temperature. Charge-transfer complexes of polymers of high molecular weight (polyvinylcarbazole with $\bar{M}_n$ = 460 000, polystyrene with $\bar{M}_n$ = 10 000–860 000) have equilibrium constants which increase with rise in temperature (Fig. 5). The occurrence of conformational transitions in polystyrene, polyvinylcarbazole, and their charge-transfer complexes in solution is confirmed by the temperature dependence of the dielectric loss angle. For the temperature variation of the conformation of polymers and the effect of these conformational transitions on complex formation these workers conclude that the van't Hoff method for calculating change in enthalpy during complex formation is incorrect when high molecular weights characterise one or both components. Methods ensuring isothermal experimental conditions, e.g. microcalorimetry in solution, must be used to determine the enthalpies of such processes.

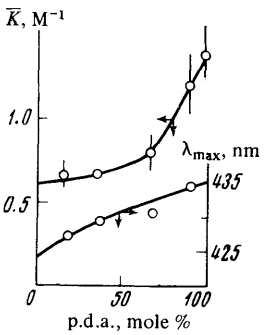


Figure 4. Dependence of $\bar{K}$ and λ_{max} of charge-transfer complex of styrene–*p*-dimethylaminostyrene copolymer with maleic anhydride on composition of copolymer in benzene as solvent[134].

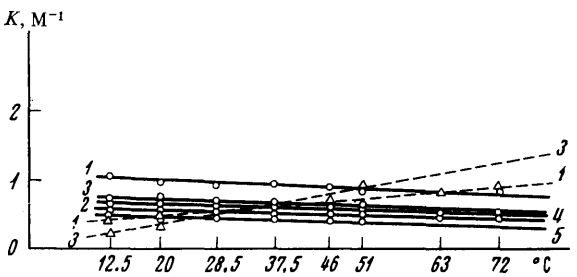


Figure 5. Temperature dependence of equilibrium constants in dichloroethane of charge-transfer complexes of polyvinylcarbazole varying in molecular weight M_n: –o–) 30 000; –Δ–) 460 000 with several acceptors: *1*) tetracyanoethylene; *2*) 7,7,8,8-tetracyanoquinodimethane; *3*) chloranil; *4*) bromanil; *5*) fluoranil[135].

Kinetic investigations of polymeric charge-transfer complexes have begun recently. Boudevska and Neitchev[137] used the "stopped flow" spectrometric method to study the kinetics of complex formation by tetracyanoethylene with polyvinylcarbazole, poly(naphthyl methacrylate), and the corresponding simple analogues in chloroform solution. All the complexes showed high rate constants ($\sim 10^4$ + M^{-1} s^{-1}), which were independent of the molecular weight of the donor. The rate constants of complex formation by tetracyanoethylene with polyvinylcarbazole and with *N*-ethylcarbazole were somewhat higher than with poly(naphthyl methacrylate) and naphthyl methacrylate, from which it was concluded that the rate of complex formation depended on the electron-donating power of the complexing unit.

The reversibility of the equilibrium of polymeric donor-acceptor complexes can be utilised for the chromatographic separation of complicated mixtures of chemical compounds, in particular to separate nitrated polystyrene[125].

Table 2.

Donor	Donor concn., M	Acceptor	Acceptor concn., M	K_{eq}, M^{-1}	ε_{max}	$\delta_0 - \delta_{AD}$ n.m.r.	Solvent	Ref.
N-Ethylcarbazole	$4.0\cdot10^{-2}$—$9.6\cdot10^{-2}$	tetracyanoethylene	$2.0\cdot10^{-3}$	5.85 20°	1090			130
Polyvinylcarbazole	$3.1\cdot10^{-2}$—$6.2\cdot10^{-2}$	tetracyanoethylene	$8.0\cdot10^{-3}$	1.3	1060		dichloromethane	
N-Ethylcarbazole	$3.0\cdot10^{-2}$—$2.4\cdot10^{-1}$	tetracyanoquinodimethane	$1.0\cdot10^{-3}$	2.87	2770			
Polyvinylcarbazole	$3.0\cdot10^{-2}$—$1.2\cdot10^{-1}$	tetracyanoquinodimethane	$2.0\cdot10^{-3}$	1.19	1310			
N-Ethylcarbazole		tetracyanoethylene		10.8 25°	1460			
Polyvinylcarbazole		tetracyanoethylene		2.9	1245			
N-Ethylcarbazole		trinitrobenzene		2.75		1.821	chloroform	65
Polyvinylcarbazole		trinitrobenzene		1.5 25°				
N-Ethylcarbazole	$0.26\cdot10^{-2}$—$1.0\cdot10^{-2}$	tetracyanoethylene		94.1	500		chloroform	136
Polyvinylcarbazole	$0.39\cdot10^{-2}$—$1.0\cdot10^{-2}$	tetracyanoethylene		261.0	80			
N-Ethylcarbazole	$3.0\cdot10^{-2}$—$7.0\cdot10^{-2}$	tetracyanoethylene	$3.0\cdot10^{-3}$	5.25 20°	927			
Polyvinylcarbazole (30 000)	$3.0\cdot10^{-2}$—$1.2\cdot10^{-1}$	tetracyanoethylene	$5.0\cdot10^{-3}$	0.94	1250		dichloroethane	135
Polyvinylcarbazole (460 000)	$9.0\cdot10^{-2}$—$2.0\cdot10^{-1}$	tetracyanoethylene	$1.0\cdot10^{-1}$	0.15 20°	1820			
NN-Dimethyl-*p*-toluidine*		chloranil		1.75	1490		benzene	134
Poly-*p*-dimethylaminostyrene		chloranil		4.38	610		benzene	
Poly-*p*-dimethylaminostyrene	$2.0\cdot10^{-2}$	chloranil	$2.0\cdot10^{-2}$	2.77	785			
Poly-*p*-dimethylaminostyrene		dichlorodicyano-*p*-benzoquinone	$2.5\cdot10^{-4}$	$3.89\cdot10^{4}$	5700		benzene	133

* Model compound of poly-*p*-dimethylaminostyrene.

Thus the main lines of research on polymeric charge-transfer complexes have been connected with applied problems of semiconductor technology and electrography, with the physical chemistry of the formation and behaviour of the complexes in solution. Microcalorimetry and nuclear magnetic resonance, ultraviolet, visible, and infrared spectroscopy have been used to study the polymeric complexes[138]. Thermodynamic parameters calculated by the van't Hoff method and obtained for the same polymeric complexes in different laboratories do not agree (Table 2). Since macromolecules in solution may undergo complicated conformational transformations depending on the temperature and influencing the thermodynamics of complex formation, all thermodynamic characteristics of such processes will be functions of temperature, so that the van't Hoff method for determining enthalpies cannot be accepted as valid. Microcalorimetric methods must be used, enabling heats of formation to be determined under isothermal conditions. The main problem—the relation between the equilibrium constants of the polymeric complexes and those of their low-molecular analogues—is not always definitely solved. It is quite likely that such a state of quantitative data on polymeric charge-transfer complexes is due to a series of inaccuracies in the generally accepted methods for determining equilibrium constants. We shall therefore examine briefly the general principles of the calculation of equilibrium constants for complex formation in solution.

V. GENERAL PRINCIPLES OF THE CALCULATION FROM SPECTROPHOTOMETRIC DATA OF THE EQUILIBRIUM CONSTANTS OF CHARGE-TRANSFER COMPLEXES

In the investigation of charge-transfer complexes in solution, where they may undergo dissociation, the observed parameters characterise not the individual complex but an equilibrium mixture with the starting materials. Several monographs have been published on methods for the investigation of equilibrium mixtures[5,139–141]. When only one equilibrium

$$q[D] + p[A] \rightleftarrows [D]_q[A]_p \qquad (8)$$

is established, the problem of the simultaneous determination of physicochemical parameters and equilibrium constants has been solved for the simplest and most frequent case of unit coefficients $p = q = 1$.

On the assumption of unit activity coefficients of all species present in solution, the equilibrium constant expressed in molar concentrations is

$$K = \frac{[AD]}{[D][A]} . \qquad (9)$$

The material balance of the system is represented by the relations

$$[A]_0 = [A] + [AD] , \qquad (10)$$

$$[D]_0 = [D] + [AD] , \qquad (11)$$

where $[A]_0$ and $[D]_0$ are the initial concentrations of the components A and D. If the optical density D is additive, we have

$$D = \varepsilon_{AD}[AD] + \varepsilon_A[A] + \varepsilon_D[D] + \varepsilon_S . \qquad (12)$$

Equations (9)–(12) contain five unknowns—[A], [D], [AD], ϵ_{AD} and K_{AD}—for the spectrophotometric case. Only simultaneous solution of equations for two experimental points obtained under different concentration conditions will enable ϵ_{AD} and K_{AD} to be determined. Owing to the cumbersome form of the equation obtained, various approximations are used depending on the stability of the complex.

For weak complexes Eqns. (9) and (12) reduce to a single equation containing the two unknowns ϵ_{AD} and K_{AD}. The coefficients ϵ_A and ϵ_D are determined experimentally, and then simplifying functions concerning the experimental conditions are introduced to bring this equation to a form which can be solved graphically. The simplifying condition in the deduction of the Benesi–Hildebrand equation

$$\frac{[A]_0}{D} = \frac{1}{K_{AD}\cdot\varepsilon_\lambda^{AD}}\cdot\frac{1}{[D]_0} + \frac{1}{\varepsilon_\lambda^{AD}} \qquad (13)$$

is that $[D]_0 \gg [A]_0$. This method[142] requires extrapolation to concentrated solutions. Scott[143] suggests the preferable variant

$$\frac{[D]_0[A]_0}{D} = \frac{[D]_0}{\varepsilon_\lambda^{AD}} + \frac{1}{K_{AD}\cdot\varepsilon_\lambda^{AD}} \qquad (14)$$

which entails extrapolation to dilute solutions for the estimation of ϵ_λ^{AD} and K_{AD}. Several modifications of Eqn. (13) are available depending on specific experimental conditions[143–147].

All approximate methods yield[148] an overall equilibrium constant K relating to all the isomeric equimolecular complexes, including contact complexes, together with an average extinction coefficient.

$$K_{AD} = \Sigma K_i \ , \qquad \varepsilon_\lambda^{AD} = \Sigma K_i \varepsilon_{\lambda i} / K \ . \tag{15}$$

The concept of contact complexes or contact charge transfer was introduced by Orgel and Mulliken[148] to explain the discrepancy arising in the relation between equilibrium constants and extinction coefficients. Mulliken had remarked[19] that increase in the equilibrium constant should be accompanied by an increase in the quantum-mechanical dipole moment and in the oscillator strength of the transition in the transfer of charge. A corresponding strengthening of the charge-transfer band may be expected[149]. However, the calculated equilibrium constants and extinction coefficients for weak complexes show the opposite relation[150]. Orgel and Mulliken suggested that the exchange of electrons occurring in the absorption of light could occur not only between donors and acceptors combined in a complex but also on the random collision of the free donors and acceptors. The weaker the complex the more significant the contribution of contact charge transfer to the total absorption by the complex. When the whole of the absorption characteristic of donor–acceptor interaction results from contact charge transfer, the Benesi–Hildebrand method yields $K = 0$ and $\epsilon = \infty$. Thus the chief defects of approximate graphical methods of calculation for weak systems are due to the "conspiracy of errors effect", when the total experimental inaccuracies distort the true values of K and ϵ[151–155].

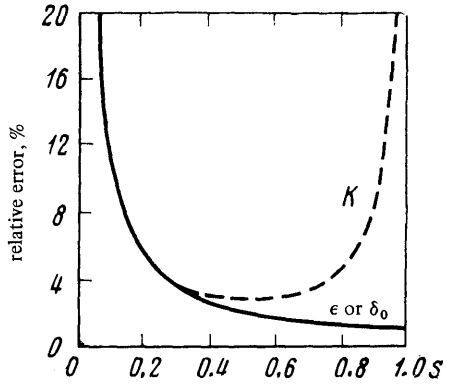


Figure 6. Dependence of relative error on concentration ratio S of components[162].

The literature on weak charge-transfer complexes has recently been overflowing with critical investigations of two-parameter equations used to determine equilibrium constants and extinction coefficients[156–163], in which various criteria of reliability were suggested for determining equilibrium constants of weak complexes. Person, for example, stated[161] that the most accurate values are obtained when the concentration of the donor lies in the range (0.1 to 9)K^{-1}. At donor concentrations below $0.1K^{-1}$ graphical solution of Eqns. (13) and (14) will give negative values. Derenleau[162] analysed theoretically the minimum error as a function of the concentration ratio S of the components, and showed that the most reliable values of K and ϵ are formed in the range $S = 0.2–0.8$ (Fig. 6). This diagram shows also that the relative errors for experiments conducted within the range $S = 0.01–0.1$ will correspondingly vary by 100–101%, and attempts to obtain accurate values of K and ϵ by a graphical method are meaningless.

Further, as shown above, the deduction of the Benesi–Hildebrand equation assumes the presence of only one equilibrium, but the linearity of Eqn. (13) by no means implies the absence of a complicated equilibrium[164,165]. This simplification may lead to inadequacy of the suggested reaction mechanism and of the equation describing the reaction.

VI. USE OF ELECTRONIC COMPUTERS TO CALCULATE COMPLEX-FORMATION EQUILIBRIA IN POLYMER SYSTEMS

A method of trial and error entailing use of an electronic computer has recently been suggested, in contrast to approximate methods for estimating equilibrium constants and extinction coefficients. A graphical variant is Drago's method[166], in which arbitrary component concentrations are chosen and appropriate equilibrium constants are calculated for each series of experiments, after which graphs are plotted of equilibrium constant against extinction coefficient. In the ideal case the lines representing all series of experiments should intersect in a single point, which gives the true values of K and ϵ. However, such a procedure is extremely laborious.

The method of trial and error using a computer[167–172] has several advantages over approximate methods: a solution can be found for complexes other than equimolecular, approximation becomes unnecessary, and the restriction to the extremal conditions $[D]_0 \gg [A]_0$ is removed. For example, Conrow[168] finds the concentration of the complex from initial calculation of the equilibrium constant. This concentration is then used to find the most suitable value of the extinction coefficient ϵ^{AD} in Eqn. (12). The required equilibrium constant K and extinction coefficient ϵ are found by calculating the absorption at every experimental point and accumulating the sums of the squares of differences between calculated and experimental values. The computation is terminated when the change in the difference

$$F_{min} = \sum_{i=1}^{N} (D_{calc.} - D_{exp.})^2 \tag{16}$$

becomes arbitrarily small. The non-linear methods described for calculating equilibrium parameters have hitherto been applied to systems of low molecular weight[167–172]. The complexity of the equilibrium of polymer systems due to the possible presence of several complexes and the irreproducibility of published data make resort to electronic computers necessary.

The method of minimisation of the function for polymer systems has hitherto been applied only to solutions of complexes of poly(phenyl methacrylate), poly(naphthyl methacrylate), polyvinylcarbazole, and their model analogues

with tetracyanoethylene[136]. Equimolar initial concentrations of the components were taken, and the reaction was thus regarded as a simple one-stage formation of an equimolecular complex. However, the values obtained[136] for the equilibrium constants were hundredfold the usual values, which is inconsistent with our ideas on weak complexes. Furthermore, the relations between equilibrium constants for polymeric and low-molecular complexes were opposite to those found by Rembaum[130] and by Smets[65].

The survey of methods for investigating charge-transfer complexes in solution reveals the complexity of the study of equilibrium complex formation in polymer systems, where the usual phenomena for the simple complexes (contact charge transfer) are accompanied by the specific behaviour of chain molecules (variation in configuration of the macromolecule, mobility of the chain, etc.).

The study of complex formation between polymeric donors and low-molecular acceptors obviously requires further deepening of research using the latest achievements of physicochemical methods and of calculations by means of electronic computers.

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Promotion of Aluminosilicate Catalysts by Reactants and Additives

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Experimental results are given on the promotion of aluminosilicates—amorphous and crystalline—by components of the reaction mixture (alkenes, halogen-containing compounds) and by molecules (water, nitrogen, carbon dioxide, etc.) not involved in the reaction stoichiometry. The effect of additives or reactant molecules on the catalyst depends on their structure and composition, as well as on the concentration of the promoter. A suggested mechanism of promotion of aluminosilicates and zeolites is considered. A list of 160 references is included.

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I. INTRODUCTION

Artificial and naturally occurring aluminosilicate catalysts and zeolites (constructed on an aluminosilicate frame) have found wide use in the petroleum-processing and petrochemical industry for the cracking of petroleum fractions, the alkylation of aromatic hydrocarbons, the polymerisation of alkenes, the isomerisation of alkylated aromatic hydrocarbons, *trans*-alkylation, and other processes[1-5]. The aluminosilicate catalysts are built of interconnected polyhedra such as $[AlO_4]$, $[AlO_5]$, and $[AlO_6]$ groups and the $[SiO_4]$ tetrahedron. They contain also hydroxy-groups and water molecules, either sorbed or structural. In zeolites aluminium is present in $[AlO_4]$ tetrahedra "stabilised" in the lattice by $[SiO_4]$ tetrahedra and by other groups. "Isolated" $[AlO_4]$ tetrahedra present in the structure of aluminosilicates and zeolites are the most active in catalysing the reactions of hydrocarbons, alcohols, and other compounds[6,7]. Zeolites are used also as matrices in the production of new zeolite-containing catalysts possessing excellent operating properties.

The efficiency of the industrial or laboratory conversion of various hydrocarbons and other compounds depends not only on the composition and structure of the catalyst but also on the composition of the initial mixture of reactants under otherwise similar experimental conditions, i.e. temperature, pressure, type of process, duration of continuous operation of the catalyst, and other variables. The activity of solid catalysts can be increased considerably (promoted) by the addition of reactant molecules or by introducing non-reactants into the reaction mixture. Such enhancement of the activity of a catalyst by oxygen molecules was first observed for liquid-phase hydrogenation[8]. In the Soviet Union work on the promotion of catalysts by reactant molecules was undertaken by Roginskii[9], who suggested that promotion of the solid surfaces was due to change in their structure and electronic state, departure of their compositions from stoichiometric, and the trapping of the promoting additives in surface defects on a metallic or oxide solid catalyst. More recently the idea has developed that promotion involves action on a solid surface by molecules of a promoter acting as a non-stoichiometric component in the catalysis[10]. This concept is phenomenological in character, like the ideas of variation in composition and properties of the catalyst under the influence of the reaction mixture[11] and like the deductions based on the formal kinetics of the interaction of a catalyst with reactant molecules[12].

The above paper[10] gave several examples of the activation of various catalysts by components of the reaction mixture or by molecules of substances specially added thereto. However, no systematic survey has been made of information on the change in activity and selectivity of aluminosilicates, varying in composition and structure, under the influence of reactant molecules or on the control of the activity and selectivity of catalysts by changes in the composition of the reaction mixture. It has now been shown that certain compounds present in a hydrocarbon reaction mixture promote the action of an aluminosilicate when they are present at certain concentrations, but deactivate the catalyst when present at other concentrations. Roginskii termed this phenomenon *modification*, and the additives themselves *modifiers*[9].

II. PROMOTION OF ALUMINOSILICATES BY ALKENES IN CRACKING, ALKYLATION, POLYMERISATION, AND HYDROGEN EXCHANGE

It was established as early as 1948 that alkenes act as promoters[13] in the isomerisation of hydrocarbons in the presence of halide catalysts. Later it was observed[14] that small (0.1—0.35 mole %) additions of octene to the reaction mixture on the cracking of n-octane enhance the activity of an aluminosilicate catalyst, with an increase in the conversion of the alkane approximately from 21% to 27%. Additions of more than 0.4 mole % of the alkene diminish the quantity of n-octane decomposed (Fig. 1): i.e. the catalyst is deactivated. The alkene itself may undergo partial conversion. However, it had undergone repeated preliminary involvement in the main process.

Experiments in which 0.27 mole % of radioactive ethylene $^{14}C_2H_4$ was added to the reaction mixture were made in order to obtain a more precise idea of the mechanism of the action of the alkene on the catalyst and on the conversion of n-octane. Radiometric analysis established[14] that at most 20% of the ethylene mixed with octane underwent transformation, and the molecular ratio of conversion of the former to that of the latter was ~1 : 100. This suggests that the effect of the alkene molecules is to change the energy state both of the catalytic centres and of the reactant molecules. The behaviour of alkene molecules mixed with alkanes and a catalyst probably differs from their behaviour in the purely thermal cracking of hydrocarbons, where unsaturated hydrocarbons inhibit breakdown of saturated hydrocarbons, which occurs by a radical—chain mechanism[15].

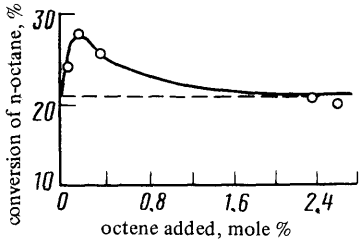


Figure 1. Effect of additions of unsaturated compounds on the cracking of n-octane at 518°C for 18 s. The broken line represents a blank experiment.

The promotion of an aluminosilicate catalyst by extremely small quantities (<0.01%) of alkenes was observed in the alkylation of aromatic hydrocarbons by alcohols[16-22]. Table 1 shows that, if a starting material isolated from the products of catalysis (which may contain alkenes) is subjected to alkylation, the yields are higher than those from the alkylation of the pure raw material (alkenes were detected by treating the catalysate with bromine water or potassium permanganate solution)[22].

Small additions of alkenes to the reaction system have a favourable effect on the hydrogen—deuterium exchange between isobutane and deuterium oxide in the presence of an aluminosilicate catalyst[23]: the rate of exchange in the presence of 0.5 vol.% of isobutene in the mixture was higher than in the absence of the alkene, although the activation energy of exchange was 17 kcal mole^{-1} in both cases. After alkenes had been removed from the mixture by hydrogenation, the rate of exchange decreased nearly to one-third[23] or exchange ceased completely[24] at high temperatures, in spite of the presence of alkenes.

Alkenes formed during the dehydrogenation of alkanes promote a catalyst containing platinum. Thus pure n-pentane does not undergo isomerisation in the presence of pure alumina under 7 atm at 220°C.[25] If a small quantity of platinum is deposited on the aluminium oxide, rapid isomerisation takes place. It was assumed[25] that platinum causes the formation of a small quantity of an alkene (or a carbonium ion), which is now able to isomerise on the acid carrier and again be hydrogenated to an alkane. We may suppose that the alkene itself is able to promote the platinum—alumina catalyst and enhance its isomerising activity.

Nevertheless, some alkenes tend to inhibit the conversion of others[26,27]. In the presence of an aluminosilicate catalyst containing nickel monoxide, for example, the polymerisation of ethylene is inhibited by 3—5% of propene or butene in the mixture. Yet the isomerisation of cyclopropane in the presence of an aluminosilicate or a cobalt oxide—aluminosilicate catalyst gives far higher yields in the presence of added ethylene or propene than in the absence of alkenes[28].

Table 1. Alkylation of benzene, toluene, phenol, bromobenzene, and chlorobenzene by propan-2-ol with a space velocity v = 0.2 cm^3 cm^{-3} h^{-1} at 250°C*.[22]

Molar C_6H_6R reactant ratio	Yield of alkylation products, mass%									
	cumene		cymenes		isopropylphenol		isopropylbromobenzene		isopropylbenzene	
	I	II	I	II	I	II	I	II	I	II
2:1	29.6	29.8	39.0	40.8	39.0	—	16.5	19.5	13.0	14.5
4:1	53.0	58.6	60.0	62.6	58.0	58.7	31.0	37.0	31.0	33.0
6:1	59.0	64.6	74.0	80.2	63.5	73.9	38.0	45.0	33.0	39.5
8:1	60.2	68.5	74.3	82.5	70.0	—	42.0	53.5	40.0	50.5
20:1	73.5	94.0	79.5	96.3	81.0	98.0	69.0	92.0	63.3	81.0

*(I) Fresh starting material; (II) starting material isolated from products of catalysis.

The above experimental results obviously indicate that small doses of alkenes added to a reaction mixture act as promoters of aluminosilicates. The optimum content of alkenes exerting an activating effect on catalytic centres is probably below 1%. Higher concentrations of alkenes usually tend to deactivate the catalyst, as shown by a decrease in the rate of the process.

III. PROMOTION OF ALUMINOSILICATES BY "INERT" CHEMICAL COMPOUNDS

It has been established experimentally that water, carbon dioxide, and other molecules added in certain quantities to the reaction mixture are able to promote aluminosilicates, zeolites, and γ-alumina in the reactions of hydrocarbons and other compounds or else to change their adsorptive capacity[29-51]. In turn, heating aluminosilicates and zeolites to a certain temperature enhances their activity towards deuterium—hydrogen exchange[41], polymerisation[7], cracking[29], etc.

The activity of an artificial aluminosilicate catalyst towards the cracking of cumene[29,30] varies with the quantity of water introduced into the system, passing through a maximum whose position depends on the composition of the catalyst, its method of preparation, and the drying conditions[52]. Thus Kaliko and Pervushina[30] first heated an aluminosilicate catalyst in a vacuum at 700°C for 700 h, then cooled it in the vacuum to 400°C, and passed cumene vapour through it. If the catalyst were absolutely dry, it exhibited no catalytic activity on contact with isopropylbenzene. The adsorption of 0.00035 mass % of water conferred considerable activity on the aluminosilicate, which increased with the sorption of additional quantities to reach a maximum at 0.2 mass % of water. Similar results were obtained when an aluminosilicate was treated with caesium hydroxide solution, ignited at 750°C, and then treated with water[30].

Table 2 shows that the catalytic activity of an aluminosilicate in the cracking of cumene passes through a maximum with variation in its water content[53]. This was attributed[54] to variation in the relative quantities of protic and aprotic centres. The promotion of aluminosilicates by water has been observed also [31,32,35] in cracking, isomerisation, deuterium–hydrogen exchange[24,51], and polymerisation[55].

Table 2. Effect of dehydration on the activity of an aluminosilicate catalyst in the cracking of cumene[53].

Time of treatment of catalyst at 700°C, h	Water remaining in catalyst, mass %	Relative activity
Initial	1.40	1
12	1.63	1
15	0.53	1.3
30	0.42	2.1
40	0.37	1.7
50	0.16	1.6

The reactions undergone by 2,2,3-trimethylpentane, 2-methylpentane, and n-heptane in the presence of an aluminosilicate catalyst, with and without addition of water to the reaction vessel, are mainly of the cracking and isomerisation type[48]. The activity of the catalyst passes through a maximum at different quantities of water vapour absorbed by the aluminosilicate in the two reactions: maximum cracking and isomerisation were observed with 2,2,3-trimethylpentane, 2-methylpentane, and n-heptane with water contents in the catalyst of respectively 0.1, 0.047, and 0.15 mass %. The results for the isomerisation of 2-methylpentane were identical with those of Ref. 26. With rise in temperature from 162 to 180 and then to 200°C the yields of products from n-heptane for the "dry" catalyst were respectively 7.53, 21.83, and 52.83 [%]; the corresponding yields for the "wet" catalyst (with the optimum water content of 0.1 mass %) were 44.30, 53.41, and 77.23 [%].

Table 3. Effect of water (supplied at 0.03 $cm^3\ cm^{-3}\ h^{-1}$) on yield of xylenes from the isomerisation of *m*-xylene fed at 0.3 $cm^3\ cm^{-3}\ h^{-1}$.[56]

Temp., °C	Yields, mass %			
	toluene	*m*-xylene	*p*-xylene	*o*-xylene
400	trace	67.8	14.7	9.3
450	2.5	51.1	16.7	18.5
470	9.7	47.2	12.5	17.5
450	3.7	55.0	13.6	13.6 (no water)

Aluminosilicates exhibited their maximum activity when they had adsorbed 0.05 mass % of water[31]. Yet the addition of water vapour[56] to ethylene diminishes its rate of polymerisation in the presence of an aluminosilicate catalyst containing nickel monoxide, and the yield of products of the isomerisation of *m*-xylene and its dismutation into toluene increases on the introduction of water into the reaction system (Table 3).

Nitrogen and carbon dioxide also promote aluminosilicates, as was observed in a study by a pulse method of the disproportionation of toluene[57] in currents of these gases in gas–liquid chromatographic apparatus. The kinetic results were processed quantitatively by the method of Refs. 58 and 59. The rate of disproportionation of toluene was higher in nitrogen than in hydrogen, as is shown by the equations—in a stream of hydrogen

$$K \cdot k = 34 \cdot 10 \exp(-30\,000/RT)$$

and in a stream of nitrogen

$$K \cdot k = 0.2 \cdot 10^{-1} \exp(-20\,000/RT)$$

where k (in s^{-1}) is the rate constant and K (atm^{-1}) the adsorption equilibrium constant. These indicate that conducting the disproportionation in hydrogen increases the activation energy, whereas in nitrogen fewer catalytically active centres function, but the process has a smaller activation energy. Thus hydrogen molecules slightly deactivate the aluminosilicate, whereas nitrogen molecules activate it. The pre-exponential factor is proportional to the number of active centres[60]. These results are supported also by data[61] on the polymerisation of hex-1-ene on aluminosilicate catalysts containing cobalt oxide. Thus the yield of liquid polymerisation products in the presence of hydrogen at 190°C is 7.6%, which rises to 22.6% when 7.0 vol.% of carbon monoxide is added. Crystalline aluminosilicates are promoted also by carbon dioxide[62,63].

IV. PROMOTION OF ALUMINOSILICATES BY GASEOUS HYDROGEN HALIDES

Artificial and native aluminosilicate catalysts were activated by pretreatment in a gaseous halogen or by a continuous supply of a hydrogen halide to the reaction zone. If a stream of gaseous hydrogen chloride is passed through a mixture of benzene, propene, and a catalyst, for example, alkylation can be effected with high yields at temperatures below the boiling point of benzene[64]. It is interesting that alkylation takes place more efficiently when the catalyst has first been completely dehydrated at temperatures above 500°C..

Gaseous hydrogen chloride also increases the yield when benzene is alkylated by alkyl halides at relatively low temperatures. This indicates that hydrogen chloride is a promoter of aluminosilicates in different reaction media, so that promotion is probably not due to formation of a protonated centre but to additional activation of the catalytic polyhedra.

In the absence of hydrogen chloride hardly any alkylation of benzene by ethylene occurs on aluminosilicate catalysts right up to 500°C.[65] Introduction of the gas into the stream of benzene and ethylene leads to an appreciable rate of alkylation to give a yield of 0.285 mole of ethylbenzene per mole of ethylene (at 450°C, with liquid benzene supplied at 0.075 mole $cm^{-3}\ h^{-1}$). Such alkylation is described[65] by the kinetic equation for a second-order irreversible heterogeneous reaction. The temperature dependence of the rate constant is

$$k = 2.77 \cdot 10^3 \exp(-90\,100/8.313T)\ . \qquad (1)$$

Increase in activity of an aluminosilicate on the addition of gaseous hydrogen chloride to the reaction mixture has been observed also in the isomerisation of n-butene[66] and in the alkylation of toluene by propene[67,68]. In these experiments the aluminosilicate had undergone preliminary treatment

with the gas for 1 h. The alkylation was conducted with molar proportions of toluene and propene of 2.3 : 1, a rate $v = 1.1$ cm^3 cm^{-3} h^{-1}, and the catalyst functioning at 200°C for 1 h.

Table 4. Alkylation of toluene by propene[67,68].

Reaction products	Yields (× 100), mole mole^{-1}			
	aluminosilicate activated with HCl (gas)			Unactivated aluminosilicate
	initial	first regeneration	second regeneration	
Cymenes (total)	26.5	25.8	29.1	22.0
o-Cymene	23.5	25.0	23.4	25.8
m-Cymene	36.0	34.2	36.8	33.4
p-Cymene	40.5	40.7	39.8	40.8
Di-isopropyltoluenes	22.1	20.2	21.1	13.7
Hexenes	17.9	14.2	14.6	13.2

Table 4 shows that the high activity of an aluminosilicate treated with gaseous hydrogen chloride is preserved even after several cycles of regeneration in a current of air at 550°C for 3 h, but that the products of the alkylation of toluene by propene on activated aluminosilicates contain more *m*-xylene than is obtained with unactivated catalysts.

Other results[69,70] confirm the stable character of the centres produced in aluminosilicates by the action of gaseous hydrogen chloride. It was suggested[71] that the effect of the gas was to increase activity by forming more active centres than in the original aluminosilicate. Experimental data on the change in catalytic activity indicate that a gaseous hydrogen halide transforms $[AlO_n]$ polyhedra in the surface layer of the catalyst into polyhedra of mixed type $[AlO_nHal_m]$, with a change both in the composition of the polyhedron and in its acceptor power ($n = 1-6$ and $m = 1-3$). The $[AlO_4]$, $[AlO_5]$, $[AlO_6]$, and $[AlO_nH_m]$ polyhedra may undergo a change not only in symmetry and composition but also in energy state, which may influence the stability of intermediate complexes of reactant molecules with catalytic centres, and hence favour easier conversion of the reactant molecules.

V. PROMOTION OF ALUMINOSILICATES BY ALKYL HALIDES AND OTHER HALOGENATED COMPOUNDS

The alkylation of aromatic hydrocarbons by alkyl halides in the presence of aluminosilicates gives higher yields than do the pure alkenes[72-78]. This may be due to higher reactivity of the alkyl halides and to the promoting effect of these compounds themselves or of their decomposition products[79] on the catalytic centres of the aluminosilicates.

Carbon tetrachloride exerts a strong promoting effect on aluminosilicates in the alkylation of benzene by ethylene[80]: thus the temperature dependence of the rate constant in its absence is

$$k = 1.41 \cdot 10^{-6} \exp(-10\,000/RT) \qquad (2)$$

but on the addition of 0.3 mass % CCl_4 this becomes

$$k_1 = 2.63 \cdot 10^{-6} \exp(-10\,600/RT) \ . \qquad (3)$$

These results show an increase in rate of alkylation of some 80% in the presence of carbon tetrachloride. The higher pre-exponential term in the latter equation suggests that the intermediate complex of the catalytic centre with reactant and promoter molecules is "looser" than in the absence of tetrachloromethane, while the energy state of the complexes is almost the same in the two cases. Experimental results for the promotion of a catalyst by carbon tetrachloride are listed in Table 5. Termination of the supply of carbon tetrachloride to the reaction mixture results in a sharp decrease in the conversion of ethylene in the alkylation of benzene, whereas in the presence of 0.3 mass % CCl_4 raising the pressure and the molar ratio of benzene to ethylene increases the proportion of starting material converted.

Table 5. Effect of quantity of tetrachloromethane on conversion of ethylene on aluminosilicate catalyst under 20 atm at 250°C with molar velocity $n_0 = 0.0357$ mole g^{-1} h^{-1}*.[80]

Tetrachloromethane added to benzene, mass %	Conversion of ethylene, %
0.0	35
0.1	42
0.2	50
0.3	75
0.5	75

* Molar ratio of benzene to ethylene $\gamma = 2.7 : 1$.

It is interesting that aluminosilicates differing in composition are unequally activated by an alkyl halide (ethyl chloride) in the alkylation of benzene by ethylene. Fig. 2 shows that an aluminosilicate containing 30 mass % Al_2O_3 + 70 mass % SiO_2 is most strongly promoted by ethyl chloride or its decomposition products. These results will be explained[81-83] in Section VIII.

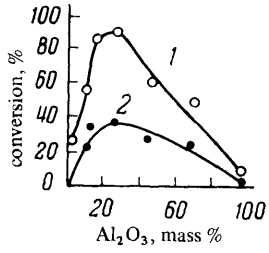


Figure 2. Activity of aluminosilicate catalysts, differing in composition, in the alkylation of benzene by ethylene with the addition of ethyl chloride (benzene supplied at $n_0 = 0.0357$ mole g^{-1} h^{-1} under 3.0 atm): 1) 0.3 mass % C_2H_5Cl added to benzene; 2) pure $C_6H_6 + C_2H_4$ mixture.

The character and the magnitude of the effect of alkyl halides on aluminosilicate catalysts depend also on the composition and structure of the compound introduced into the reaction mixture. Table 6 shows that hydrocarbons in which geminal hydrogen atoms have been replaced by halogen atoms activate aluminosilicates more strongly than do their isomers with a different arrangement of

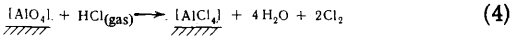
halogen atoms. The greater the number of geminal halogen atoms in a compound, the stronger usually is its promoting action on a catalyst. Compounds containing bromine or fluorine atoms have a weaker activating effect on an aluminosilicate than have compounds containing only chlorine atoms. Halogen-containing compounds of vicinal structure generally lower the activity of an aluminosilicate catalyst towards alkylation.

Table 6. Alkylation of benzene by ethylene in presence of an aluminosilicate catalyst (containing 16 mass % Al_2O_3) with $\gamma = 2.7:1$ and $v = 1.2$ cm^3 cm^{-3} h^{-1} at 300°C.[80]

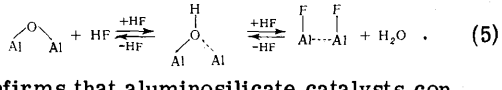
Halogenated compound	Quantity added to benzene, mmoles $(100\ g)^{-1}$	Ethylene converted, %	Ethylbenzene in products, %
CCl_4	1.95	93.5	96.5
$CHCl_3$	2.50	77.8	90.8
CH_2Cl_2	3.52	47.0	83.2
C_2H_5Cl	4.65	89.5	96.0
C_2H_5Br	2.75	68.9	89.0
CBr_4	0.90	61.4	88.2
1,1,1-$C_2H_3Cl_3$	2.25	71.4	96.5
1,1,2-$C_2H_3Cl_3$	2.25	31.2	64.1
1,1-$C_2H_4Cl_2$	3.03	55.2	97.5
n-C_3H_7Cl	3.81	52.5	94.8
i-C_3H_7Cl	3.81	58.4	95.2
1,2-$C_2H_4Cl_2$	3.03	18.1	66.2
1,2-$C_3H_6Cl_2$	2.66	25.2	—
$FCCl_3$	2.18	83.4	98.3

The data in Table 6 suggest that the promoting or deactivating effect of additives on a catalyst is due to undecomposed hydrogen halide molecules. However, decomposition products of halogenated compounds—alkenes and hydrogen halides—may play some part. The activity of an aluminosilicate catalyst towards the conversion of hydrocarbons passes through a maximum depending on the quantity of alkyl halide added to the reaction mixtures[67,68]. Thus in the alkylation of toluene by propene under 1 atm at 240°C the maximum growth in activity of the catalyst was obtained on addition of 1.4 vol.% of isopropyl chloride to the reaction mixture. Gaseous hydrogen chloride and propene were detected among the reaction products. This confirms that aluminium silicate can be promoted in a high-temperature reaction not only by the reactant molecules but also by gaseous hydrogen chloride and by an alkene. It is assumed also that hydrogen chloride molecules can be sorbed by catalytic centres of the aluminosilicate, thereby displacing products or impeding the sorption of compounds responsible for the formation of "carbon" and other highly condensed products. This preserves accessibility to catalytic centres for the initial reactant molecules and thereby maintains high catalytic activity in the aluminosilicate for a longer time. This suggestion has found confirmation[84,85].

It is also possible that polyhedra of novel chemical composition may be formed by interaction between gaseous hydrogen chloride molecules and the aluminium—oxygen polyhedra:



(4)



(5)

Scheme (4) confirms that aluminosilicate catalysts containing fluorine but no hydroxy-groups[86] are extremely active in the isomerisation and the polymerisation of hydrocarbons, despite the diminished acidity of the centres. The appearance of centres of the type AlO_nHal_m in an aluminosilicate under the influence of gaseous hydrogen chloride is indicated by data on the isomeric composition of products of the alkylation of toluene by propene in the presence of an aluminosilicate catalyst and aluminium chloride. Table 7 shows that increase in the isopropyl chloride content of the mixture in the presence of the catalyst is accompanied by an increase in the *m*-cymene content of the products, until the equilibrium concentration is reached. A similar pattern is observed with rise in temperature of the alkylation of toluene by propene in the presence of aluminium chloride. The increase in the *m*-cymene content of the mixture in the former case is probably due to an increase in the number of halogenated catalytic centres formed in the aluminosilicate by scheme (4), which affect the isomerisation of *o*- and *p*-cymenes into the *meta*-isomer. This is evident from the fact that the composition of the cymene fraction in the former case approaches the composition obtained in the presence of aluminium chloride.

Table 7. Isomeric composition of products of the alkylation of toluene by propene.

Catalyst	*T*, °C	Molar toluene/propene ratio	Isopropyl chloride added, vol.%	Cymene fraction, %			Ref.
				ortho	*meta*	*para*	
Aluminosilicate	240	3.32:1	—	20.2	38.9	40.9	67
		3.54:1	1.43	15.1	44.9	40.0	67
		4.74:1	6.0	10.0	52.5	37.5	67
		3.56:1	100*	10.0	52.4	37.6	67
Aluminium chloride	100	—	—	18.9	48.1	33.0	87
	80	—		25	43	25	87
	20	—	—	17	44.2	38.8	88

* Alkylation by pure isopropyl chloride.

The promoting action of halogenated compounds—not of their decomposition products—on the catalytic centres of aluminosilicates can be revealed by an investigation at relatively low temperatures, at which the molecules of the halogenated compounds remain unchanged.

VI. PROMOTION OF ALUMINOSILICATES IN LOW-TEMPERATURE REACTIONS

Examples of low-temperature reactions are the polymerisation of pentenes and the liquid-phase alkylation of benzene by propene. In the presence of aluminosilicate catalysts quite high rates of polymerisation are observed[89-93] even between −20 and +60°C, with 60—70% conversion. The activity of an artificial catalyst can be further enhanced by the action of carbon tetrachloride introduced into the reaction mixture. In Fig. 3 the relative conversion of a mixture of pentenes is plotted against the quantity of tetrachloromethane added to the mixture[79]. Every point was obtained from the dependence of the yield of reaction products on time of contact at 20°C. Fig. 3 shows that the addition of up to 0.5 vol.% of carbon tetrachloride to the reaction mixture increases the proportion of pentene converted by roughly 50%.

Dichloroethane and diethyl ether have a similar effect on aluminosilicates[79]. Addition of 0.2 mass % of the former or 0.1 mass % of the latter increases the yield of polymerisation products from a mixture of pentenes at room temperature by 100—200% in comparison with the pure pentenes. Fig. 4 shows that the activity of the catalyst depends on the quantity of dichloroethane or ether added to the reaction mixture, and may pass through a maximum. In the presence of dichloroethane the activity of a promoted catalyst is higher than that of an unpromoted catalyst at all the concentrations studied. With ether, however, increasing its quantity above an optimum value entails strong deactivation of the catalyst. This indicates that alkyl halides and ether have different effects on the aluminosilicate centres and on the reactants.

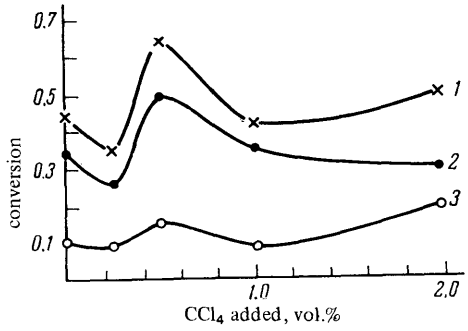


Figure 3. Effect of quantity of carbon tetrachloride added on the polymerisation of a mixture of isopentenes at 20°C for 120 min: 1) conversion of monomers; 2) yield of dimers; 3) yield of trimers.

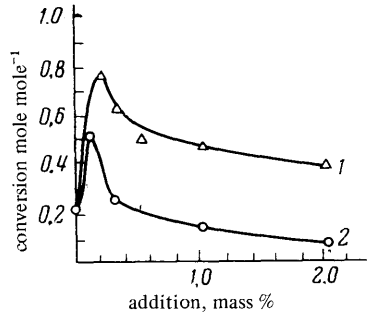


Figure 4. Dependence of conversion of a mixture of isopentenes at 20°C with time of contact 130 min on quantity of: 1) 1,2-dichloroethane; 2) diethyl ether.

Industrial aluminosilicate catalysts (including those containing zeolites) are contaminated by compounds of sodium, potassium, calcium, and other cations, which may have diverse effects on the catalytic activity[93,94]. Alkali-metal ions usually lower the activity of aluminosilicates towards the conversion of hydrocarbons. Halogenated compounds enhance considerably the activity of catalysts containing alkali-metal ions, probably in polyhedra of the type $[MO_4]$. This applies to reactions of hydrocarbons both at high and at low temperatures.

Aluminosilicates containing sodium and potassium ions are obtained by treatment with aqueous solutions of the chlorides[95]. Table 8 summarises results on the polymerisation of pentenes in the presence of such catalysts at 20°C, with and without the addition of carbon tetrachloride to the reaction mixture. It shows that aluminosilicates containing sodium and potassium ions exhibit less intense catalytic activity towards the polymerisation of pentenes than do those not containing such ions, and that potassium ions deactivate the catalyst more strongly than do sodium ions. The addition of 0.5 vol.% of tetrachloromethane to the reaction mixture almost completely restores the activity of a "poisoned" aluminosilicate, a potassium aluminosilicate being promoted more strongly than the sodium compound.

Table 8. Initial rates of polymerisation of a mixture of pentenes at 20°C.[95]

Soln. to treat catalyst	CCl_4 added, vol.%	Initial rate (× 10⁴) of conversion, moles g^{-1} h^{-1}	Soln. to treat catalyst	CCl_4 added, vol.%	Initial rate (× 10⁴) of conversion, moles g^{-1} h^{-1}
—	0	3.37	1.0*N* NaCl	—	1.33
—	0.25	2.57	0.3*N* NaCl	0.5	2.53
—	0.5	4.57	0.5*N* NaCl	0.5	2.96
—	1.0	3.24	1.0*N* NaCl	0.5	2.30
—	2.0	1.78	0.1*N* KCl	—	0.21
0.1*N* NaCl	—	2.44	0.1*N* KCl	0.5	3.21
0.5*N* NaCl	—	1.44			

An aluminosilicate treated with sodium chloride solution exhibits low catalytic activity also towards the alkylation of benzene by propene[96]. With a molar ratio of benzene to propene of 2.56 and v = 0.44 cm^3 cm^{-3} h^{-1} at 320°C the yield of isopropylbenzene is 38.7%, which falls to 3.7% on an aluminosilicate catalyst poisoned by sodium ions. The introduction of 3 mass % of propyl chloride into the reaction mixture with the "poisoned" aluminosilicate enables the yield to be raised again to 20.5%.

Thus halogenated compounds promote aluminosilicates both in high-temperature reactions of various hydrocarbons and in low-temperature reactions. The halogen compounds activate not only ordinary industrial aluminosilicate catalysts but also catalysts that have been "poisoned" by alkali-metal salts and other compounds.

VII. PROMOTION OF ZEOLITES

Original papers and reviews have been published on the structure of zeolites[97,98] and on their catalytic activity[99-103], showing that the latter depends on the nature, composition, and structure of the crystal lattice, as well as on the type of cations present in the polyhedra[104-106]. Alkali-metal ions usually deactivate a zeolite towards the reactions of hydrocarbons, and change the selectivity in isomerisation and in other reactions; but ions of bivalent and tervalent metals enhance the catalytic activity of zeolites. The activity of zeolites of various types can be changed (increased or decreased) by introducing into the hydrocarbon mixture halogen-containing compounds[71], carbon dioxide[115], certain organic acids, and other compounds of donor[96] or acceptor type.

Thus an NaY-type zeolite does not catalyse the transformation of hydrocarbons, in particular the isomerisation of *o*-xylene into *p*- and *m*-xylenes, at temperatures below 500°C.[107] Addition of gaseous hydrogen chloride up to a partial pressure of 0.05 gauge atm in the stream of hydrocarbons ensures 10% conversion of *o*-xylene, which can be increased to 15% by raising the partial pressure to 0.1 gauge atm. A zeolite of type MnY can be promoted for the alkylation of toluene by methanol when gaseous hydrogen chloride is supplied continuously into the flow of reactants (Fig. 5).[108]

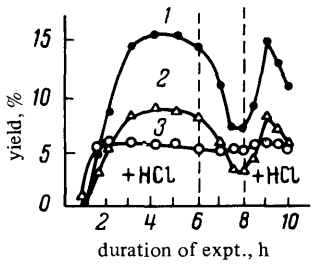


Figure 5. Effect of gaseous hydrogen chloride on activity of MnY-type zeolite in the alkylation of toluene by methanol ($\gamma = 2:1$) at 225°C as shown by yields (%) of: 1) *p*-xylene; 2) *m*-xylene; 3) *o*-xylene.

The activity of an NaX-type zeolite[109] is determined by the partial pressure of gaseous hydrogen chloride and depends on the degree of exchange of sodium for calcium or cerium(III) ions. When such ionic substitution reaches 30%, the zeolite is not activated by gaseous hydrogen chloride. The yield of cumene formed by alkylation is increased from 15% to 25% when 40% of the sodium ions in the zeolite have been replaced. Some of the hydrogen chloride molecules are strongly sorbed, while others are weakly sorbed. The rate of reaction is assumed to be proportional to the number of weakly sorbed molecules, which are responsible for promoting the zeolite.

The action of hydrogen bromide, water, and hydrogen chloride molecules on the catalytic centres in an REX-type zeolite (RE = rare-earth element) in the alkylation of benzene by ethylene can be traced from published data[110]. The zeolite was first ignited at 400°C and kept in a vacuum of 0.2 mmHg for 0.5 h, after which hydrogen bromide, water, or hydrogen chloride (1.85 mg-equiv.g^{-1}) was introduced into the system, and benzene was alkylated with ethylene at 177°C ($C_6H_6 : C_2H_4 = 12$ and $v = 8.5\ s^{-1}$). Fig. 6 shows that, with short times (<50 min) of contact of the reaction mixture with the zeolite, the sequence of activating effects of the additives is $HCl > H_2O > HBr$; on prolonged (>100 min) operation of the zeolite this sequence changes to $H_2O > HBr > HCl$; and if the catalyst had operated for <25 min, added water and hydrogen bromide tended to deactivate the catalytic centres. It may be supposed that the catalytic centres on the fresh zeolite already possess the highest activity, so that the above three polar molecules are first sorbed on them. This leads to some diminution in acceptor power and hence in catalytic activity of the $[AlO_4]$ tetrahedron. With increase in duration of operation of the zeolite its catalytic centres become covered with condensation products of high molecular weight or "carbon". Under these conditions the sorption of water, hydrogen bromide, or hydrogen chloride on them preserves[110,111] their enhanced catalytic activity in the transformation of hydrocarbons.

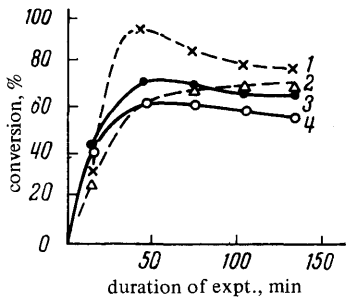


Figure 6. Variation of activity of REX-type zeolites with additions of: 1) H_2O; 2) HBr; 3) HCl; 4) pure zeolite.

Faujasite of NaY type is completely inactive in the cracking of cumene[112]. Quite high activity results from the introduction of gaseous hydrogen chloride, when the yield of cracked products is proportional to the surface coverage of the catalyst with the halide. It is assumed that a new catalytic centre is formed[113]:

$$M^+Z^- + HCl \rightleftarrows \begin{matrix} M^{+\delta'} \ldots Z^{-\delta''} \\ | \qquad\quad | \\ Cl^{-\delta_1} \quad H^{+\delta_2} \end{matrix}$$

However, the increased chlorine content of the mixture[114] is insufficient to increase the activity of the zeolite significantly. The formation is probably necessary of centres with a definite structure and composition, i.e. a definite polyhedron, e.g. $[AlO_nCl_m]$. Polyhedra of this type have been detected by nuclear magnetic resonance when a zeolite is treated with chlorine at high temperatures[115].

The activity of zeolites, like that of aluminosilicates, can be enhanced by the action of alkyl halides and other compounds[96]. Table 9 shows that propyl chloride promotes zeolites of types NaX, NaY, CaX, and HX, but tends to deactivate CaY. The activity of a zeolite passes through a maximum, whose height and position depend on the type of zeolite, with increase in the quantity of propyl chloride added to the reaction mixture. The HX zeolite is almost twice as active as CaX towards the alkylation of benzene by pure propene. When propyl chloride is added to the reaction mixture, the yields of cumene on CaX approach those on an HX type. The NaY zeolite does not catalyse the alkylation of benzene by pure propene, but a markedly different picture is obtained when 3.0 mass % of propyl chloride is added to the system: the yield of cumene is then 0.173 mole per mole of the alkylating agent, which increases to 0.55 mole $mole^{-1}$ in the presence of 10 mass % of propyl chloride (calculated on the benzene). The alkylation of benzene by pure n-propyl chloride gives a yield of isopropylbenzene of only 0.104 mole $mole^{-1}$.

It is interesting that the activity of zeolites used in the alkylation of benzene by propene to which propyl chloride has been added remains fairly high after regeneration.

As mentioned above, this effect is connected with the appearance of new polyhedra in the zeolite under the influence of decomposition products of alkyl halides. The activity of the promoted zeolite diminishes after several regeneration cycles, but remains above that of the initial zeolite. This indicates that regeneration of a promoted zeolite by atmospheric oxygen and other molecules entails the breakdown of a number of chlorine-containing catalytic centres.

Table 9. Alkylation of benzene by propene with additions of propyl chloride and propan-2-ol under atmospheric pressure at 320°C.[96]

Alkylating agent and promoter, mass % on benzene	Rate of supply of benzene, $cm^3\ cm^{-3}\ h^{-1}$	Molar C_6H_6/C_3H_6 ratio	Yield (× 100) based on alkylating agent, mole $mole^{-1}$		
			cumene	di-isopropylbenzenes	
				meta	*ortho*
HX zeolite					
C_3H_6	0.46	2.50	19.1	2.5	1.5
C_3H_6 + 3% n-C_3H_7Cl	0.46	2.75	31.6	3.4	2.2
C_3H_6 + 10% n-C_3H_7Cl	0.45	2.52	33.2	1.8	1.1
C_3H_6 + 20% n-C_3H_7Cl	0.42	2.90	37.4	1.4	1.0
n-C_3H_7Cl	0.44	3.00	29.7	1.1	0.7
C_3H_6 + 3% i-C_3H_7OH	0.44	2.90	18.0	2.8	2.4
CaX zeolite					
C_3H_6	0.53	3.12	12.1	1.2	0.8
C_3H_6 + 0.5% n-C_3H_7Cl	0.57	3.10	21.3	2.2	1.2
C_3H_6 + 10% n-C_3H_7Cl	0.53	2.30	34.5	1.4	0.9
C_3H_7Cl	0.52	3.00	17.8	0.4	0.3
NaY zeolite					
C_3H_6	0.48	3.13	0.54		
C_3H_6 + 3% n-C_3H_7Cl	0.48	3.15	17.5	1.5	1.0
C_3H_6 + 10% n-C_3H_7Cl	0.43	2.07	55.0	2.7	1.5
n-C_3H_7Cl	0.47	3.00	10.4	—	—
Zeolite regenerated from previous expts. (C_3H_6 + 10% n-C_3H_7Cl)	0.47	2.80	32.7	4.0	2.3
Zeolite regenerated from previous expts. (C_3H_6)	0.48	2.82	23.3	8.3	1.7
CaY zeolite					
C_3H_6	0.52	3.7	50.0	3.4	1.8
C_3H_6	0.42	3.5	43.4	2.3	1.7
C_3H_6	0.42	3.0	46.5	2.2	1.1
C_3H_6 + 3% n-C_3H_7Cl	0.43	3.2	39.0	1.5	1.0
C_3H_6 + 9% n-C_3H_7Cl	0.41	2.4	26.7	1.2	0.6
C_3H_6 + 10% n-C_3H_7Cl	0.40	3.0	23.5	1.3	0.6

The activity of an NaY-type zeolite towards the alkylation of benzene by propene[98,116] depends on the molecular structure and type of additive. Table 10 shows that molecular chlorine, tetrachloromethane, n-propyl chloride, propionaldehyde, and acetone activate the zeolite. They can be arranged in the sequence

$$Cl_2 > CCl_4 > n\text{-}C_3H_7Cl \gg (CH_3)_2CO > C_3H_7CHO,$$

according to their activating effect on the zeolite. Propionic acid, nitropropane, and chlorobenzene have no activating effect on an NaY-type zeolite.

The presence of up to 3 mass % of water almost doubles the activity of zeolites also towards the cracking of isopropylbenzene[117-119], but the introduction of large quantities of water either has no effect or diminishes the activity. The activation of zeolites by carbon dioxide and by water is explained by surface protonation or by the formation of hydroxy-groups attached to silicon in the lattice, which are assumed to act as catalytic centres[118,119]. The promotion of zeolites by water has been observed also in the isomerisation of cyclopropane, the dehydration of alcohols[119,120], the disproportionation of toluene[121], the isomerisation of butenes[122] and xylenes[113], the alkylation of toluene by alcohol[123], and the polymerisation of ethylene and propene[124]. In many cases the change in catalytic activity of the zeolites when heat-treated at various temperatures depended on the quantity of residual water in the zeolite[110,111,120,123,125,126]. Promotion was explained by the action of molecules on "acidic" centres in the zeolite, although the structure of these centres and their energy state were not discussed.

Table 10. Alkylation of benzene by propene on NaY-type zeolite with various additives[116].

Alkylating agent and additive	Rate of supply of liquid benzene, $cm^3\ cm^{-3}[h^{-1}]$	Molar ratio, benzene: alkylating agent	Yield (× 100) based on alkylating agent, moles $mole^{-1}$		
			cumene	di-isopropylbenzenes	
				meta	*ortho*
C_3H_6	0.42	2.55	0.36	—	—
C_3H_6+3% n-C_3H_7Cl	0.485	3.15	17.3	1.5	1.0
C_3H_6+10% n-C_3H_7Cl	0.435	2.07	55.0	2.7	1.5
n-C_3H_7Cl	0.47	3.00	10.4	0.3	—
C_3H_6 (5th regeneration)	0.47	2.8	32.7	4.0	2.3
C_3H_6 (6th regeneration)	0.47	2.82	25.3	3.2	1.7
C_3H_6	0.468	3.03	0.96		
C_3H_6+3% C_3H_7CHO	0.455	3.20	2.0		
C_3H_6+3% C_3H_7COOH	0.420	2.36	0.8		
C_3H_6+0.5 $C_3H_7NO_2$	0.487	2.72	0.8		
C_3H_6+3% CH_3COCH_3	0.45	3.14	2.9		
C_3H_6+3% CCl_4	0.45	3.11	32.5	0.96	0.5
C_3H_6 (1st regeneration)	0.443	3.56	2.3		
C_3H_6+3% C_6H_5Cl	0.435	3.44	1.9		
C_3H_6+Cl_2	0.480	3.46	34.6	2.6	1.4

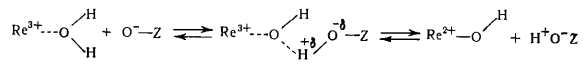
VIII. MECHANISM OF THE PROMOTION OF ALUMINOSILICATES AND ZEOLITES

Polymeric complexes, formed after adsorption of alkene molecules on catalytic centres, are assumed to play a definite part in the mechanism of the promotion[127-130] of aluminosilicate catalysts by alkenes. These hydrocarbons (propene, butenes) undergo rapid transformation with formation of a polymeric complex on an "acidic" centre of the aluminosilicate having degrees of polymerisation of 2–5.

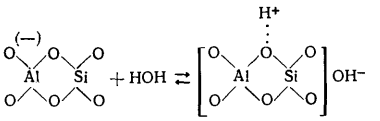
To establish the role of polymeric complexes in catalysis on aluminosilicates experiments were made on the isomerisation of but-1-ene[130] on an aluminosilicate containing polymeric perdeuteriobutene on the catalytic centre. On such a centre isomerisation yielded a large quantity of products in which the hydrogen atoms had been replaced in considerable number by deuterium. Yet hydrogen–deuterium exchange with an aluminosilicate surface that had undergone exhaustive deuteriation was comparatively small.

At low partial pressures of the alkene its degree of polymerisation in the complex is small and the activity of the catalyst also low. Both degree of polymerisation and catalytic activity increase with rise in partial pressure. Hence the effect of an alkene on an aluminosilicate catalyst depends on its degree of polymerisation with complex formation on an "acidic" centre. The optimum degree of polymerisation of ~3 units ensures the most active catalyst. The promotion of an aluminosilicate by an alkene may lead also to a change in the mechanism of isomerisation of alkenes, which is probably anionic at not very high temperatures.

The promoting effect of water molecules on aluminosilicate catalysts and zeolites is usually attributed to their ability to supply protons[131] to the surface. The transfer of protons is caused by the polarising effect of the cations, e.g. of a rare-earth metal, replacing ions in the zeolite:



A proton appears in the aluminosilicate catalyst by the mechanism



According to these schemes the catalytically active centre is a proton of a hydroxy-group attached to aluminium[131] or to silicon[35,66]. Nevertheless, direct experimental evidence has been published that the catalytically active centres in high-temperature and low-temperature reactions of hydrocarbons are aluminium—oxygen polyhedra[71,81,91,132-138], while the hydroxyl proton is able only to strengthen the accepting power of these polyhedra[137]. Furthermore, it is well known that silica has a high content of Si—O—H groups (even after ignition at temperature above 500°C), while their catalytic activity in the conversion of hydrocarbons is almost zero.

The promotion of zeolites by carbon dioxide is presumably[62,115] due to chemisorption of its molecules by sodium or calcium ions with activation of the catalytic centre. Chemisorption of carbon dioxide on a zeolite is regarded[115] as increasing the number of protons per unit surface, and hence enhancing the catalytic activity.

Kaliko and Pervushina[29,30] assume that water in aluminosilicates is present in both structural and adsorbed forms. Promotion is effected only by molecules adsorbed on catalytic centres. Catalysis of the conversion of hydrocarbons by aluminosilicates is supposed to involve active Lewis centres (aluminium three-coordinated with oxygen) or Brønsted centres[33]. However, such a view of the structure of the catalytic centre is incomplete and inconsistent with the geometrical limits of stability of the polyhedra. A coordinated triangle of type $[AlO_3]$ is unstable in aluminosilicates[139]. The ratio of the radii $r_{Al}/r_O = 0.418$ characterises the stability of $[AlO_4]$ and $[AlO_6]$ polyhedra. Triangular coordinated groups are stable only when this ratio is 0.15—0.22. The value 0.418 is the lower limit of stability of a coordinated octahedron. Hence only $[AlO_4]$ tetrahedra and $[AlO_6]$ octahedra are able to exist in aluminosilicates. The presence of such groups has been demonstrated in native aluminosilicates[97], artificial aluminosilicates, and zeolites[139,140].

Absorption of a water molecule is assumed to convert a Lewis centre into a Brønsted centre, a source of a proton which may be captured by hydrocarbon (e.g. alkene) molecules with formation of a carbonium ion, converted into the final products with regeneration of a proton. However, such an interpretation leads to difficulties in explaining the mechanism of the conversion of alkanes. Furthermore, it was shown experimentally that the activity of an aluminosilicate catalyst passes through a maximum with increase in the quantity of water introduced into the reaction zone, although most of the "aprotic" centres remain unoccupied by water molecules[141,142]. Danforth postulates[143] that water in an aluminosilicate acts as a cocatalyst, moving from centre to centre if the latter are contiguous. This results in displacement of the hydrocarbon from the complex catalyst and facilitates regeneration of the catalytic centre.

It must again be noted that heating aluminosilicate catalysts above 800°C leads to irreversible loss of their catalytic activity. The activity cannot be increased by addition of any quantity of water, so that the promotion of aluminosilicates involves catalytic centres having a different structure, which will be discussed below.

A convincing explanation of the promotion and deactivation of catalytic centres in aluminosilicates varying in type, structure, and composition was based on the view[71,81,91,132-138] that $[AlO_4]$ and $[AlO_6]$ polyhedra act as catalytic centres, with $[AlO_4]$ tetrahedra distributed as "islands" in a solid lattice, probably of defect (unsymmetrical] structure, catalytically the more active. Among artificial aluminosilicates the highest concentration of such tetrahedra is found in a catalyst containing 35—40 mass % of alumina and 65—60 mass % of silica[82]. Aluminosilicates of various compositions may contain "isolated", "island" $[AlO_4]$ tetrahedra, "condensed" $[AlO_4]$ tetrahedra, and "isolated" and "condensed" $[AlO_6]$ [octahedra].[82,83] The above aluminosilicate contains the maximum number of "isolated" $[AlO_4]$ tetrahedra. Artificial and natural aluminosilicates containing the largest number of such tetrahedra possess the greatest catalytic activity[134-138,144,145].

The degree of promotion of aluminosilicates by halogenated hydrocarbons depends on their alumina and silica contents[80]. Maximum promotion by ethyl chloride is observed[80] precisely with aluminosilicates containing 35—40 mass % of alumina, possessing maximum activity, and containing the maximum number of $[AlO_4]$ tetrahedra of "island" type. These results suggest that the promotion of aluminosilicates by halogenated and other compounds depends firstly on the content of $[AlO_4]$ tetrahedra of "isolated" type, secondly on the change in structure of the catalytic centre, and thirdly on the change in energy state of the catalytic centre and the reactant molecules.

The promotion of aluminosilicates by water, carbon dioxide, nitrogen, and other molecules may be attributed to a change in the acceptor properties of the $[AlO_4]$ tetrahedron or the $[AlO_nH_m]$ polyhedron in general, and to a change in the occupancy of unfilled $3d$ levels, possibly also in the symmetry of the tetrahedron. With small quantities of water, carbon dioxide, nitrogen, and other activating molecules sorbed on the catalyst surface the acceptor power of the catalytic aluminium—oxygen polyhedron may be increased by a change in the energy level of a vacant $3d$ orbital, which facilitates polarisation of a carbon—hydrogen bond in the hydrocarbon molecule, its cleavage, and reaction by a definite mechanism.

Andrianova and Roginskii considered[14] that the conversion of hydrocarbons on catalysts, whether promoted or not, had a radical—chain mechanism. Hansford[37] suggested a carbonium-ion mechanism, but this was not confirmed[142].

The promotion effect when halogen-containing compounds interact with catalytic centres in a zeolite or an aluminosilicate containing alkali-metal ions as $[MO_n]$ polyhedra (n = 4--6) can be attributed primarily to the action of the promoter molecule on the state of this polyhedron. Hence the increase in the activity of the catalyst under the influence of activating molecules may be due to the electronic (orbital) promotion of surface centres. The same phenomenon may occur under the influence of reactant molecules, with additional excitation of the catalytic centre. Interaction of activator with reactant molecules may further excite the latter. When activating

molecules of acceptor type interact with alkenes or with aromatic hydrocarbons, charge-transfer complexes are formed[146]. Such a complex has been observed with a mixture of chloroform and benzene[147,148].

Stepwise transfer of excitation energy along a layer of reactant and additive molecules sorbed on the catalyst surface may also occur. This is confirmed by the fact that a considerable proportion of benzene and carbon tetrachloride molecules (3% and 13% respectively) are already in excited vibrational states at room temperature[149]. This excitation may be transmitted to catalytic centres or reactant molecules and may promote these centres, changing their energy state and destroying the symmetry.

New catalytic centres resulting from chemical substitution may play some part in activating the catalyst[150]. Treatment of aluminosilicates or alumina with hydrogen halides produces Brønsted centres[151,152]. Partial replacement of hydroxy-groups by halogen atoms may also occur, with the formation of new active centres of Lewis[153] or Brønsted [154] type. However, treating aluminium oxide with fluorine compounds diminishes the acidity of the surface, while the catalytic activity towards the conversion of hydrocarbons increases sharply[155,156]. As mentioned above, the charge-transfer complexes themselves, e.g. that of an alkyl halide with an aromatic hydrocarbon, may have a considerable effect on the catalytic activity of the $[AlO_n]$ polyhedra. Transfer of charge may be effected from a 3*d* orbital of the halogen to a vacant π-orbital of the aromatic hydrocarbon or conversely; some compounds of this type are able to promote, whereas others deactivate, the catalytic centres.

Mixing benzene with molecules of considerable acceptor power, such as tetrachloromethane, hydrogen chloride, chloroform, and perchloroethane, yields associated charge-transfer complexes[157-159]. Associated complexes can be formed only with a certain acceptor concentration in the mixture, e.g. when the concentration of hydrogen chloride or chloroform does not exceed 0.02 mole per mole of benzene, above which concentration the resulting complexes already dissociate. The composition of the complex depends on the concentration of the solution. The stability of the complexes is connected not only with charge transfer but also with the stepwise migration of a proton. The latter is governed by the thermal motion and force fields of the benzene molecules.

Aromatic hydrocarbons mixed with ammonia, ether, dioxan, and other compounds of the same type form complexes in which the former act as acceptors and the latter as donors. Here the hydrocarbons have the role of aprotic acids, and the other reactants that of bases. These results can be related to the conversion, in the presence of aluminosilicates, of hydrocarbons mixed with acceptor or donor additives.

Certain acceptor additives to the reaction mixture may enhance the activity of aluminosilicates. Their activating effect, ability to form complexes with hydrocarbons, and promoting action are interrelated, as has been observed in the low-temperature[79,93,95] and high-temperature[68,116,104] reactions of hydrocarbons.

Donor molecules added in certain amounts to a reaction mixture usually lower the activity of aluminosilicates, although activation by donor molecules may be observed. Molecules of the reaction mixture may have a synergistic effect on the aluminosilicates in both cases: adsorption of a hydrocarbon on an aluminosilicate surface may lead to the formation of both radical-cations and radical-anions[160], the former by electron transfer from a molecular orbital of the donor molecule to a vacant atomic or molecular orbital of an aluminium—oxygen polyhedron, and the latter by electron transfer from a donor aluminium—oxygen polyhedron to a vacant molecular orbital of the hydrocarbon molecule. These centres may be adjacent, and it was assumed[160] that a donor catalytic centre contains an excess of oxygen atoms and favours conversion of an acceptor molecule into a radical-anion. With simultaneous or successive sorption of donor and acceptor molecules on the catalytic centres the catalytic activity of one centre may be strengthened by the other. Sorption of a donor molecule on an acceptor centre tends to strengthen the donor power of the donor centre. Conversely, sorption of an acceptor molecule on a donor centre will tend to strengthen the acceptor properties of the acceptor centre. This may be one reason why some concentrations of an additive will promote a catalyst, whereas other concentrations will deactivate it.

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Metal-catalysed Oxidation of Organic Compounds by Hydroperoxides

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Information on the oxidation of various alkenes by hydroperoxides, as well as that of nitrogen- and sulphur-containing compounds, is summarised. Aspects of the catalysis of such oxidations are considered, and their mechanism and stereochemistry are discussed. A list of 166 references is included.

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I. INTRODUCTION

The oxidising properties of hydroperoxides have long attracted the attention of research workers. Their great reactivity promises the development of highly effective methods of preparative organic chemistry and potentially successful industrial processes. We shall not attempt to survey all the reactions of hydroperoxides, especially in view of the vastness of the literature on this subject[1-7]: we shall restrict our discussion to reactions of various organic compounds with hydroperoxides in the presence of metals to yield oxidised products. Attention will be paid only to work published during the past 5–8 years. In particular, Section II will give a detailed account of the oxidation of alkenes by hydroperoxides in the presence of metals to give α-oxides, alcohols, ketones, and other oxygen-containing compounds. The mechanism and the stereochemistry of the hydroperoxide epoxidation of alkenes will be discussed.

The rest of the Review will examine hydroperoxide oxidation as an extremely promising method of organic chemistry. A reagent comprising a hydroperoxide with a metal salt resembles a peroxy-acid in its mode of action, but also exhibits several interesting novel features. Oxidations of the peroxy-acid type include the epoxidation of enol ethers, the *N*-oxidation of amines, the formation of oxaziridines from azomethines, and the oxidation of organosulphur compounds. Among reactions of a second type are the direct formation of α-hydroxyketones from alkenes, the oxidation of alcohols and quinols, the dehydrogenation of 1,4-dihydropyridines, and others.

II. EPOXIDATION OF ALKENES BY HYDROPEROXIDES CATALYSED BY METALS

1. History

Hawkins[8] discovered in 1950 that cyclohexene oxide was obtained when the cycloalkene was treated with cumenyl hydroperoxide in benzene solution in the presence of vanadium pentoxide. Under the same conditions oct-1-ene was converted into 1,2-epoxyoctane. However, the yields of the oxides were low. Their formation was explained by the addition of $RO_2^{\bullet}$ radicals at the double bond[9].

Investigation of the thermal breakdown of hydroperoxides in solutions of alkenes established[10,11] that the yields of the oxides were independent of the structure of the alkene. The effective activation energy of the reaction of oct-1-ene with t-butyl hydroperoxide was 30 kcal mole^{-1}, from which it was concluded that the reaction had a polar mechanism.

A little later the same workers[12], studying the epoxidation of oct-1-ene, 4-vinylcyclohexene, oct-2-ene, and 2,2,4-trimethylpent-1-ene by t-pentyl hydroperoxide in the presence of metal acetylacetonates, found that the highest yields of α-oxides could be obtained if the reaction were catalysed by the acetylacetonates of vanadium, molybdenum, and chromium. Significantly, the cobalt, copper, and manganese complexes were far less active. Aluminium, iron, nickel, titanium, zinc, magnesium, and zirconium acetylacetonates decompose the hydroperoxide completely, with no formation of α-oxides.

The above work formed a starting point for researches by Halcon International Inc.[13], who patented the production of α-oxides by oxidising alkenes with hydroperoxides in the presence of compounds of molybdenum, vanadium, tungsten, titanium, zirconium, tantalum, and other metals.

2. Catalysts

Compounds of molybdenum, vanadium, tungsten, and chromium are recognised to be the best catalysts for epoxidation, but even among these metals differences in activity are clearly evident. Table 1 shows the dependence on the type of catalyst of the rate and extent of the epoxidation of 2-methylpent-2-ene by cumenyl hydroperoxide[14]. The most active catalysts are hydrocarbon-soluble compounds of molybdenum, e.g. the octanoate, naphthenate[15], di-t-butylbenzoate[16], molybdic esters[17,18], and also the tetra- and para-molybdenates of pyridine and piperidine[19]. A porous ceramic obtained by sintering the oxides—alumina, silica, and molybdenum sesquioxide—has been patented as a catalyst[20]. Metallic molybdenum

can serve as catalyst when it forms the walls of the reaction vessel [21,22]. Molybdenum compounds including other active elements, e.g. heteropolyacids [23], cobalt molybdate [24], etc., have given good results.

Table 1. Epoxidation of 2-methylpent-2-ene by cumenyl hydroperoxide.

Catalyst	Time, min	Yield of oxide, %
None	930	29
$NaMoO_3$	930	70
$NaVO_3$	930	52
MoO_2	90	88
$NaSiMo_{12}O_{40}+NaMoO_3$	45	85
$MoO_2(C_5H_7O_2)_2$	45	86
$VO(C_5H_7O_2)_2$	60	75

Some patents, however, must be approached with caution. In particular, the statement that a mixture of molybdenum and nickel acetylacetonates must be used for successful epoxidation, as these catalysts are inactive when used separately [25], does not correspond to reality. Molybdenum, while more active than vanadium in the oxidation of alkenes, retreats to second place as catalyst for the epoxidation of allyl alcohols, where vanadium compounds are most active [26].

With regard to other catalysts, mention may be made of patents describing the use of compounds of tungsten [27,28] as well as of titanium, chromium, niobium, zirconium, tellurium, rhenium, and other elements [29]. It is extremely interesting that boric esters catalyse the reactions [30,31] with metaborates the most active [32]. A recent paper [33] has described the use of carbonyl and phosphine complexes of rhodium, ruthenium, and iridium as catalysts.

Table 2. Effect of solvent on oxidation of oct-1-ene.

Solvent	Conversion of t-BHP*, %	Yield of oxide, %
Ethyl acetate	100	89.3
Di-isopropyl ketone	98.7	88.0
Acetophenone	98.6	67.8
Benzene	99	63
Methanol	69.6	42.4
Acetone	50.4	23.8
Dioxan	29.6	21.2

*t-BHP = t-butyl hydroperoxide.

3. Solvents

A hydrocarbon or a tertiary alcohol is generally used as solvent for epoxidation. Primary alcohols and ketones inhibit oxidation [14]. As illustration Table 2 lists results obtained for the epoxidation of oct-1-ene by t-butyl hydroperoxide [in various solvents] in the presence of sodium molybdophosphate.

The percentage conversions of ethylbenzene hydroperoxide in the oxidation of propene varies [35] in different solvents—ethylbenzene 99, 2-phenylpropanol 98.8, methanol 54.7, ethanol 62.8, propan-1-ol 67.8, n-butanol 78.0, and n-octanol 87.5.

Thus the successful choice of solvent depends on the specific conditions and should take into account the structure of the alkene and the hydroperoxide, together with the type of catalyst.

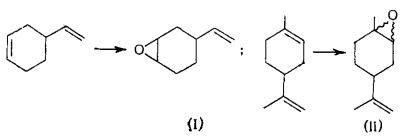
4. Effect of Structure of the Alkene and of the Hydroperoxide

Investigations on epoxidation have been reported mainly in patents and have been concerned with relatively simple alkenes. Only during the past three or four years have papers begun to appear in journals. The rate of epoxidation increases with the number of electron-donor substituents adjacent to the double bond. Table 3 illustrates the dependence of rate of oxidation on degree of branching of the alkene [14,34]. Both structural and geometrical isomers differ in reactivity. Thus the relative reactivities of *cis*-but-2-ene, *trans*-but-2-ene, and but-1-ene are 36.6, 14.2, and 1.0. [35,36]

Table 3. Oxidation of alkenes by t-butyl hydroperoxide.

Alkene	Yield of oxide, %
$C_6H_7-C(CH_3)=CH_2$	63.2
$C_6H_{11}-CH=CH-CH_3$	72.7
	76
$(CH_3)_3C=CH-CH_3$	80.5

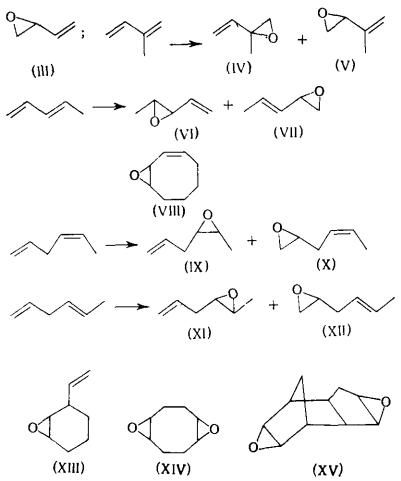
A cyclic double bond usually reacts more readily, as is shown by the epoxidation of alkenylcyclohexenes. Thus 4-vinylcyclohexene gives the theoretical yield of 1,2-epoxy-4-vinylcyclohexane (I) when oxidised with t-butyl [34], t-pentyl, or cumenyl [37] hydroperoxide. Under the same conditions *p*-mentha-1,8-dienes give the monoxides (II). [38]



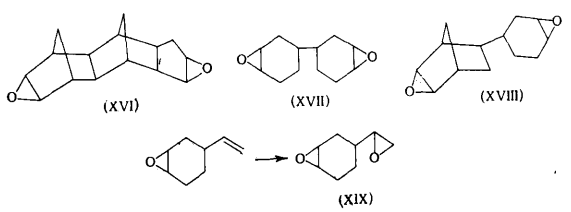
(I) (II)

Examination of the oxidation of dienes has established several empirical rules linking the completeness of oxidation with the structure of the alkene. Conjugated dienes form only monoxides [26]. Thus butadiene gives (III), [26,29] while isoprene and penta-1,3-diene form mixtures of structural isomers (IV)–(VII). [26,40] A monoxide (VIII) has been reported from cyclo-octa-1,3-diene [34]. Aliphatic 1,4-dienes, e.g. *cis*- and *trans*-hexa-1,4-dienes, are able to give only isomeric monoxides (IX)–(XII). A dioxide

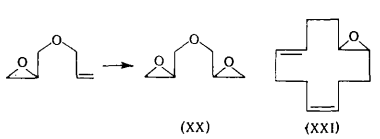
could not be obtained from 3-vinylcyclohexene, since reaction ceases at the monoxide (**XIII**) stage.



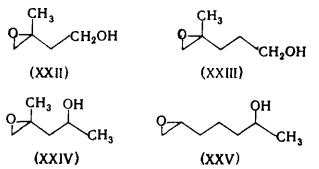
However, 1,5-dialkenes are able in most cases to react with two moles of a hydroperoxide. Cyclo-octa-1,5-diene, for example, is converted into the dioxide (XIV) by t-butyl hydroperoxide in the presence of trisodium dodecamolybdophosphate or tetrasodium dodecamolybdosilicate. The farther apart are the double bonds, the more complete is the epoxidation. This is well illustrated by bi- and tercyclopentadienes, bi(cyclohexenyl), and cyclohexenylnorbornene, which give the dioxides (XV)–(XVIII) in almost quantitative yields when oxidised by t-pentyl hydroperoxide in the presence of molybdenum pentachloride[41]. 4-Vinylcyclohexene dioxide (XIX) cannot be obtained by the direct reaction of two moles of the hydroperoxide with one mole of the diene, since the process is completely inhibited after formation of the monoxide. However, epoxidation of the latter, freed by distillation from inhibiting impurities, will give a satisfactory yield of the dioxide. The same procedure was used to obtain the dioxide of diallyl ether (XX).[26]



The oxidation of trienes by hydroperoxides has not been investigated systematically. It is known merely that *cis*,*trans*,*trans*-1,5,9-cyclododecatriene forms a monoxide (XXI).[42]



Smooth progress of the reaction is not prevented by polar groups and heteroatoms sufficiently remote from the double bond. Thus oxides of unsaturated alcohols



have been obtained by the action of t-butyl hydroperoxide in the presence of hexacarbonylmolybdenum. The best catalysts for the oxidation of allyl alcohols were vanadium compounds, but satisfactory yields of oxides can be obtained also with molybdenum catalysts (Table 4)[26]. Allylic diols are oxidised quite smoothly[26] to the oxides

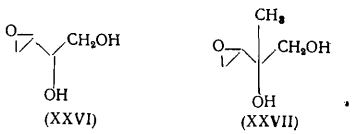


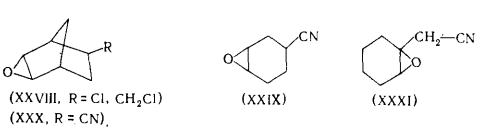
Table 4. Oxidation of allyl alcohols and ethers.

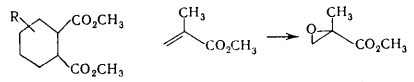
Compound*	Catalyst	Temp., °C	Time, min	Conversion of t-BHP, %	Yield of oxide, %
ROH	$Mo(CO)_6$	100	60	100	70
ROH	$V(C_5H_7O_2)_3$	100	25	92	93
$CH_2=C(CH_3)CH_2OH$	$V(C_5H_7O_2)_3$	80	30	97	100
$CH_2=C(CH_3)CH_2OH$	$Mo(CO)_6$	80	30	82	69
ROEt	$Mo(CO)_6$	95	120	73	77
R_2O	$Mo(CO)_6$	95	120	89	85
R_2O	$Mo(CO)_6$	100	180	88	58

*R = $CH_2:CH.CH_2$–.

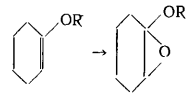
Oxidation of chlorine-containing alkenes gives yields of oxides depending on the position of the chlorine atom relative to the double bond. Thus allyl and methylallyl chlorides are converted into α-oxides in moderate yield. *trans*-1,4-Dichlorobut-2-ene is oxidised with great difficulty to give a 20% yield of the oxide[26]. However, 2-chloro- and 2-chloromethyl-norbornenes form the oxides (XXVIII) in high yield[43].

Epoxidation is not appreciably impeded by the presence of a nitrile group sufficiently remote from the double bond. In t-butyl alcohol solution at 80°C, for example, 4-cyanocyclohexene is oxidised by t-butyl hydroperoxide to give an 89% yield of the oxide (XXIX).[44] 2-Cyanonorbornene is oxidised smoothly to the oxide (XXX), and cyanomethylcyclohexene is converted not quite so well into (XXXI). Acrylonitrile is not epoxidised at all[26].





(XXXII, R = H, Me) (XXXIII)



R = Et, $COCH_3$ (XXXIV)

Few data are yet available on the epoxidation of unsaturated acids and their derivatives. However, quantitative yields of derivatives of cyclohex-4-ene-1,2-dicarboxylic acid (XXXII) have been obtained by means of t-pentyl hydroperoxide in the presence of molybdenum pentachloride or hexacarbonylmolybdenum [39,45]. A process for the epoxidation of vegetable oils has been patented, but details are not reported [46].

Mention must be made of the formation of methyl epoxymethylpropionate (XXXIII) from methyl methacrylate [26], an observation of fundamental importance, since it indicates the powerful oxidising properties of a reagent comprising a hydrogen peroxide and a molybdenum salt. Incidentally, ordinary peroxy-acids do not oxidise esters of $\alpha\beta$-unsaturated acids: only such strong oxidants as trifluoroperacetic and *m*-chloroperbenzoic acids are sufficiently reactive.

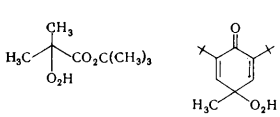
Enol ethers give high yields of oxides. Thus ethoxycyclohexene and cyclohex-1-enyl acetate are converted into the oxides (XXXIV). [47]

The influence of the structure of the hydroperoxide on the rate and the completeness of the epoxidation of alkenes has been less fully studied. Thus alkylated aromatic hydroperoxides have exhibited high activity in the epoxidation of oct-2-ene in benzene solution catalysed by hexacarbonylmolybdenum [14]. In particular, the percentage conversion of *p*-nitrocumenyl, cumenyl, and t-butyl hydroperoxides was respectively 83, 60, and 54. Hence an electron-accepting substituent in the benzene ring tends to increase the rate of oxidation.

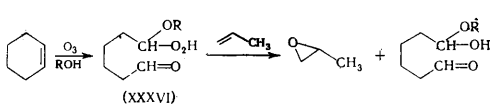
The relative reactivities of ethylbenzene, t-butyl, and cumenyl hydroperoxides in the epoxidation of propene have been given [48] as 2.4 : 1.3 : 1. t-Butyl α-hydroperoxy-α-methylpropionate (XXXV), obtained by oxidising t-butyl isobutyrate [49], is an excellent reagent for obtaining methyloxiran [50]: in the presence of molybdenum and sodium naphthenates the yield of the oxide is 78–84%.

Application of the hydroperoxides of ionol (XXXVa), di-isopropyl ketone, and tetralin has been patented [34], but their activities were not compared.

It has recently been established that smooth epoxidation of propene and cyclohexene is accomplished by means of alkoxy-ω-formylalkyl hydroperoxides (XXXVI), which are formed when cyclohexene is ozonised in solutions of primary alcohols [51].

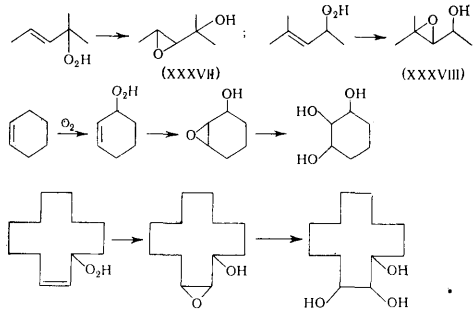


(XXXV) (XXXVa)



(XXXVI)

An interesting variety of hydroperoxide oxidation is based on the principle of the "self-epoxidation" of alkenyl hydroperoxides. In particular, the epoxyalkanols (XXXVII) and (XXXVIII) have been obtained from the hydroperoxides of 4- and 2-methylpent-2-enes:



(XXXVII) (XXXVIII)

The best catalysts for the process are compounds of tungsten [52] and vanadium [53]. Processes for obtaining cyclohexanetriols and cyclododecanetriols (above) have been based on the same principle [54,55].

5. Mechanism and Stereochemistry

Kinetic aspects of epoxidation have recently been surveyed quite fully [56]. Certain fundamental principles may be recalled here to provide a link with the above discussion. Over the range of cyclohexene concentrations 0.087–1.79 M reaction with t-butyl hydroperoxide in the presence of molybdenum acetylacetonate is initially first order with respect to the substrate and the hydroperoxide [57]. In contrast to earlier work [12] the first order with respect to the catalyst was established. Over the temperature range 24–51 °C the activation functions are $\Delta H = 12.7 \pm 0.4$ kcal mole^{-1} and $\Delta S = -19.8 \pm 1.9$ e.u. The Michaelis–Menten equation has been applied [58,59] to the initial stages of formation of an α-oxide on the basis of the considerable analogy with enzymic catalysis.

Epoxidation has been considered [57-60] to comprise the stages—(1) oxidation of the metal by the hydroperoxide to a higher (most probably the highest) valency with an increase in the number of vacant 4*d* orbitals, (2) coordination of the hydroperoxide with the catalyst involving a lone pair of electrons on an oxygen atom in the hydroperoxide and 4*d* orbitals of the metal, (3) weakening of the oxygen–oxygen bond with migration of electron density to the metal as a result of coordination, the enhancement of the electrophilic character of the hydroperoxide facilitating rupture of this bond as a result of nucleophilic attack on the alkene, (4) redistribution of the proton, (5) exchange of ligands, and (6) competitive inhibition due to the formation of catalytically inactive molybdenum–inhibitor complexes.

Epoxidation is inhibited by water, ketones, and alcohols. In particular, the inhibiting effect falls in the sequence—water, 1-phenylethanol, t-butyl alcohol, 2-phenylpropan-2-ol—and is greater the greater the stability of the molybdenum–inhibitor complex, which is determined by the nature of the inhibitor as ligand. More highly polar alcohols form more stable complexes, a relation which has been expressed quantitatively: for aliphatic alcohols the polar Taft factors σ^* were found to correlate with the dissociation constants of the complexes (Scheme 1). Thus there is no doubt about the electrophilic character of the

reaction. This conclusion was supported by a kinetic investigation of the oxidation of *para*- and *meta*-substituted styrenes, which showed that the rate-determining stage was electrophilic attack on the alkene (Table 5). This is indicated by the negative value of the constant $\rho = 1.4 \pm 0.6$.[59]

Scheme 1

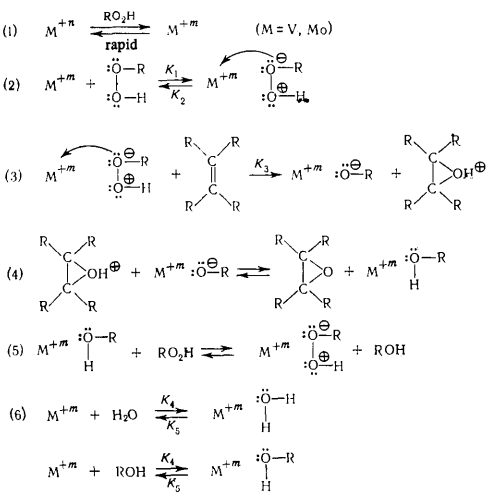
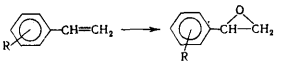


Table 5. Rate constants of the oxidation of *meta*- and *para*-substituted styrenes by t-butyl hydroperoxide

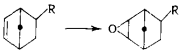


Substituent R	H	*m*-Cl	*p*-Cl	*m*-Br	*p*-Br	*m*-NO_2	*p*-CH_3
10^4 x rate constant, M^{-1} min^{-1}	26.7	21.8	30.5	26.1	31.0	3.10	89.6

The present Reviewers had found that the initial rates of oxidation by t-pentyl hydroperoxide of a series of norbornene derivatives in the presence of molybdenum pentachloride varied with the electronegativity of the 6-substituent. Table 6 shows that compounds having electron-donating substituents show higher initial rates of oxidation, whereas electron-accepting substituents lower the rate[43].

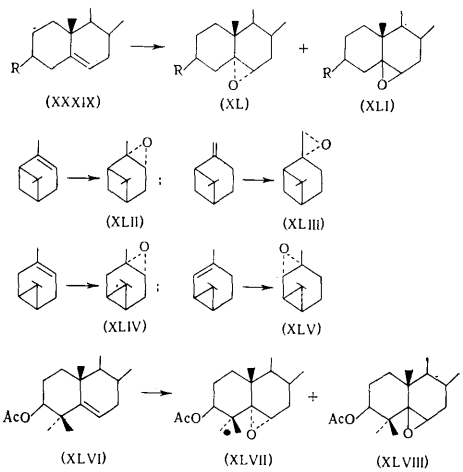
The activation energy of epoxidation can vary with the structure of the alkene and the hydroperoxide, as well as with the type of catalyst. Thus the oxidation of propene by ethylbenzene, t-butyl, and cumenyl hydroperoxides has effective activation energies of 15–15.5 kcal $mole^{-1}$,[48] but the corresponding value for the reaction between 2-methylpent-2-ene and cumenyl hydroperoxide is 23.8 kcal $mole^{-1}$.[60] The very low activation energy of 5.6 ± 0.5 kcal $mole^{-1}$ was found[43] for the reaction between norbornene and t-pentyl hydroperoxide in the presence of molybdenum(V) chloride. Introduction of an electron-accepting group into the hydroperoxide lowers the effective activation energy; in particular, a value of 11.7 ± 0.5 kcal $mole^{-1}$ was obtained[49] for the oxidation of propene by t-butyl α-hydroperoxy-α-methylpropionate [(XXXV)]. The catalyst may cause very marked changes in activation energy. In the oxidation of oct-1-ene by t-butyl hydroperoxide, for example, use of different metal acetylacetonates gave the values (in kcal $mole^{-1}$)—Cr^{III} 23, VO^{II} 15, MoO_2 12, and V^{III} 9.[12] Aspects of the mechanism of hydroperoxide epoxidation are discussed also in several other papers[61–63].

Table 6. Rates of oxidation of 6-substituted norbornene derivatives by t-pentyl hydroperoxide



Substituent R	H	CH_3	OH	OAc	*endo*-CN	*exo*-CN	CH_2OH	CH_2OAc	CO_2CH_3	Cl
$10^7 W$, $M\,s^{-1}$	35	116	7	6	9	8	23	5	2	15

An all-round assessment of a reagent is unthinkable without examination of the stereochemistry of its reactions. Among epoxidising agents the stereochemistry of epoxidation by peroxy-acids has been most widely investigated. It has been reliably established that peroxy-acids attack an alkene mainly on the less shielded side. The configuration of the resulting oxide coincides with the direction of attack by the reagent. These principles can be seen especially clearly with cyclic alkenes, such as steroids, terpenes, etc. For example, the epoxidation of Δ^5-steroids (XXXIX) by peroxy-acids produces a mixture of oxides in which the 5α,6α-isomer (XL) predominates[64,65]. Relatively slight shielding of the double bond permits the peroxy-acid to approach the opposite side also, with formation of the 5β,6β-oxide (XLI). Until recently almost nothing was known of the stereochemistry of epoxidation by hydroperoxides. It has been reported only that *cis*- and *trans*-but-2-enes formed the corresponding oxides[14].

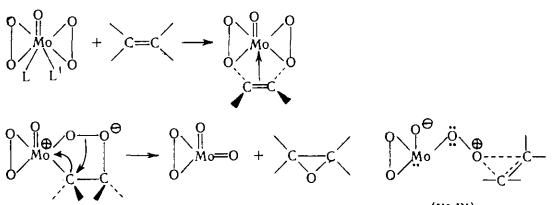


The present Reviewers investigated the stereochemistry of the epoxidation of certain steroids and terpenes[38,66], and established that it depends both on steric factors and on the presence of complexing groups in the reactant molecule. In the oxidation of unsaturated cyclic hydrocarbons and alkenes not containing these groups near the double bond

the stereospecificity of epoxidation by t-pentyl hydrogen peroxide is limited only by steric factors. Thus epoxidation of Δ^5-steroids (XXXIX: R = H, Cl, OH) occurs mainly by attack by the reagent at the less shielded α-side, which as in the experiments with peroxy-acids leads to predominance of the 5α,6α-oxides (XL) in the mixture of epimers. The bicyclic hydrocarbons—pin-2-ene, pin-2(10)-ene, car-2-ene, and car-3-ene—have such effective shielding of the double bond that, when oxidised with t-pentyl hydroperoxide in the presence of molybdenum pentachloride, only the oxides (XLII)–(XLV) are formed, whose configuration coincides with the direction of attack by the reagent. The same oxides were obtained by oxidising these monoterpenes with perbenzoic acid [66-70].

Thus epoxidation by a hydroperoxide involves a stage in which the double bond is attacked by a "molybdenum–hydroperoxide" complex, whose size governs control of the reaction solely by steric factors. This stage, it seems to us, can be modelled on the oxidation of cycloalkenes by the molybdenum pentoxide–hexamethylphosphoramide MoO_5.HMPA complex [71]. This reagent quantitatively epoxidises Δ^5-steroids (XXXIX: R = H, Cl, OH, OCOCH), to form the almost pure 5α,6α-oxides [72,73]. The above monoterpenes undergo stereospecific oxidation, being converted by this complex into the oxides (XLII)–(XLV). [74] Epoxidation by this reagent is evidently still more strictly controlled by steric factors, which follows also from experiments on 3β-acetoxy-4,4-dimethylsteroids (XLVI), also not oxidised by the reagent owing to steric hindrance by the geminal methyl groups. Hydroperoxides in the presence of molybdenum pentachloride or hexacarbonylmolybdenum are also unable to oxidise compounds of type (XLVI), whereas perbenzoic acid reacts quite readily to give a mixture of the 5α,6α- and 5β,6β-oxides (XLVII) and (XLVIII) in the proportions 82 : 18 [Table 7].

The highly stereospecific action of the MoO_5.HMPA reagent is an important argument, in the opinion of the Reviewers, for interpreting the mechanism of epoxidation as ambipolar 1,3-addition [75]. In any case, it is difficult to accept the possibility of completely stereoselective oxidation if the recently suggested [76] scheme



(XLIX)

involving a three-membered transition state (XLIX), is adopted. Anomalous results were obtained when Δ^5-steroids having oxygen-containing groups attached to $C_{(3)}$ were oxidised with t-pentyl hydroperoxide in the presence of molybdenum pentachloride (or hexacarbonylmolybdenum). Thus 3β-acetoxy-Δ^5-steroids (L) were converted mainly (55–80%) into 5β,6β-oxides. Owing to conformational distortions of rings A and B the double bond in 3-ethylenedioxy-Δ^5-steroids (LI) is accessible to attack on the β-side. Oxidation by perbenzoic acid therefore yields mainly the 5β,6β-oxides (proportions of 5α,6α- and 5β,6β-oxides 35 : 65). The ethylene acetal (LI) undergoes completely stereospecific β-epoxidation both with t-pentyl hydroperoxide in the presence of molybdenum pentachloride and with the peroxide complex MoO_5.HMPA: both reagents give the pure 5β,6β-oxides (LII).

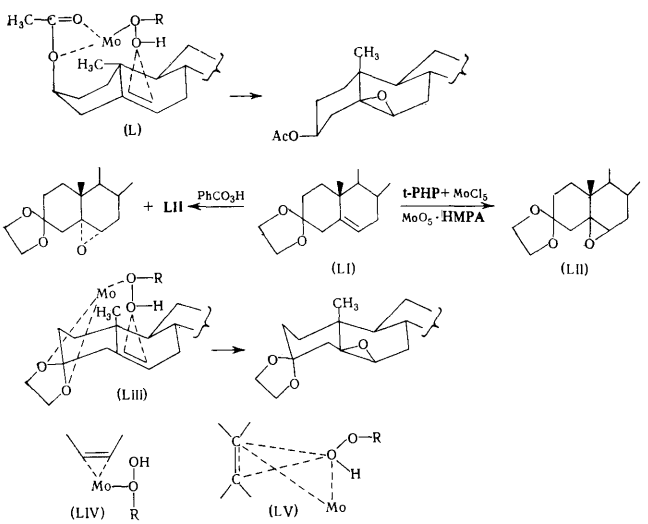


Table 7. Composition of mixtures of 5,6-oxides obtained by the epoxidation of Δ^5-steroids.

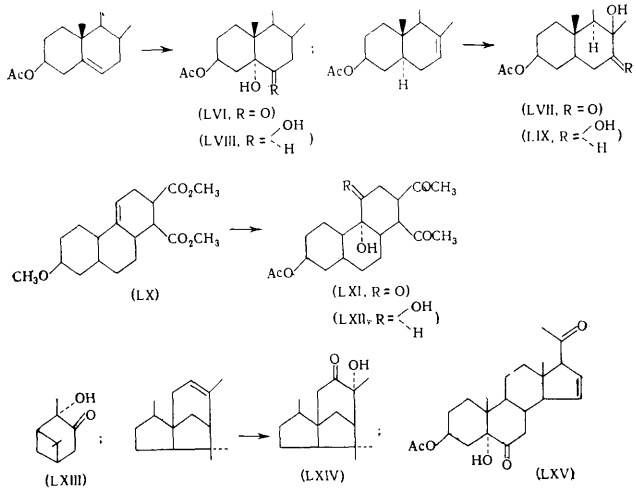
Δ^5-Steroid	Oxidising agent					
	C_6H_5COOH		t-PHP + Mo		MoO_5 + HMPA	
	5α, 6α	5β, 6β	5α, 6α	5β, 6β	5α, 6α	5β, 6β
3β-Acetoxyandrost-5-en-17-one	65	35	20	80	100	0
3β-Acetoxycholest-5-ene	70	30	45	55	80	20
3β-Acetoxyspirost-5-ene	65	35	35	65	95	5
3β-Acetoxypregna-5,16-dien-20-one	65	35	35	65	90	10
3β-Acetoxy-4,4-dimethylcholest-5-ene	82	18	no reaction takes place			
Cholest-5-ene	90	10	55	45	100	0
3α-Chlorocholest-5-ene	85	15	60	40	95	5
Cholest-5-en-3β-ol	90	10	70	30	90	10
Spirost-5-en-3β-ol	90	10	55	45	90	10
3-Ethylenedioxyspirostene	35	65	0	100	0	100

Whereas the results of epoxidation by MoO_5.HMPA can be explained by stereospecificity in the action of the reagent, the outcome of the experiments with 3-pentyl hydroperoxide and molybdenum pentachloride is somewhat unexpected. Formation of the "anomalous" 5β,6β-oxides in the oxidation of 3β-acetoxy-Δ^5-steroids and that of the "normal" 5β,6β-oxides by the epoxidation of ethyleneacetals most probably have the same origin: complexing groups combine with the metal and thereby orient the hydroperoxide for attack on the β-side. This is especially clearly evident with ethylene acetals, where steric factors and the orienting effect of the oxygen group act in harmony (LIII).

Thus the stereochemistry of the epoxidation of unsaturated cyclic hydrocarbons and of compounds containing no metal-complexing groups is determined by the direction of attack by the "metal–hydroperoxide" complex. Such attack occurs predominantly on the less shielded side and involves the formation of π-complexes of type (LIV) [63-73] or (LV). [62]

III. "HYDROXYKETONISATION" OF ALKENES

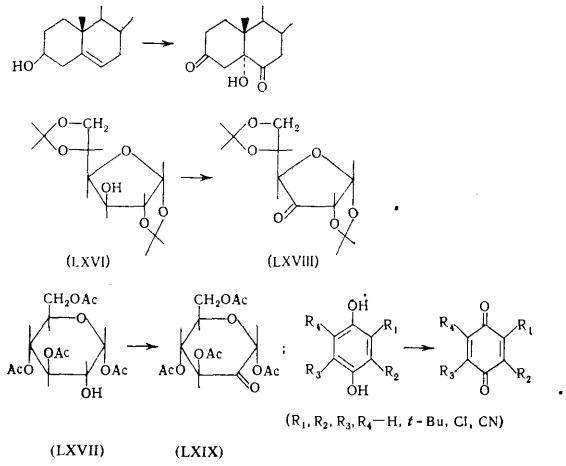
It has recently been shown [38,66,77,78] that trisubstituted alkenes can be converted directly into α-hydroxy-ketones by excess of a hydroperoxide in the presence of molybdenum, tungsten, and vanadium compounds. The yields are usually 60–90%. Thus Δ^5- and Δ^7-steroids are converted in one stage, when treated with two moles of t-pentyl hydroperoxide, into 85–90% yields of 5α-hydroxy-6-ones (LVI) and 8β-hydroxy-7-ones (LVII) respectively. The glycols (LVIII) and (LIX) were found as by-products. A double bond conjugated with an aromatic ring readily undergoes this reaction. For example, the compound (LX) gives a mixture of the hydroxy-ketone (LXI) and the glycol (LXII). It is significant that the new method enables the hydroxy-ketones (LXIII) and (LXIV) to be obtained from pin-2-ene and cedr-8-ene, whose oxides isomerise very readily [67,79].



The reaction has its limitations, since it extends only to trisubstituted alkenes. Attempts at the hydroxyketonisation of compounds containing a disubstituted double bond have been unsuccessful. Oxidation does not affect the double bond in αβ-unsaturated ketones, as is exemplified by the conversion of dehydropregnenolone acetate into 3β-acetoxy-5β-hydroxypregn-16-ene-6,20-dione (LXV).

IV. OXIDATION OF SECONDARY ALCOHOLS AND QUINOLS

Although the formation of ketones from secondary alcohols by the action of hydroperoxides is well known [80], this method has no preparative value. However, it has recently been established [38,81] that diverse secondary alcohols are easily oxidised by t-pentyl hydroperoxide in the presence of a catalyst (molybdenum pentachloride), without which hardly any oxidation occurs. The completeness of conversion varies between 40% and 90% depending on the structure of the alcohol. The new method of oxidation can be regarded as preparative in view of the high selectivity of the process. Among oxidations achieved in this way are those (percentage conversion indicated in parentheses) of cyclohexanol into cyclohexanone (95), cholestanol into cholestanone (85), 5α,22α-spirostan-3β-ol into the spirostanone (85), 18β-methyl glycyrrhetate into 3-oxomethyl glycyrrhetate (40), cholest-4-en-3β-ol into cholesten-3-one (60), *trans*-cyclohexanediol into hydroxycyclohexanone (85), pinane-2β,3α-diol into hydroxypinocamphone (80), and 3β-acetoxy-5α,6α-dihydroxysteroids into 3β-acetoxy-5α-hydroxy-6-oxosteroids (85). Oxidation of a hydroxy-group may be combined with hydroxyketonisation: thus 3β-hydroxy-Δ^5-steroids are converted in a single stage into 5α-hydroxy-3,6-diones:

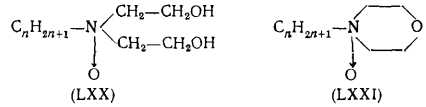


Hydroperoxide oxidation is extremely promising as a convenient method of obtaining keto-sugars [82,83], e.g. the smooth conversion of glucofuranose (LXVI) and glucopyranose (LXVII) derivatives into ketones (LXVIII) and (LXIX). Quinols are oxidised to quinones in high yields (70–95%). [38]

V. OXIDATION OF NITROGEN-CONTAINING COMPOUNDS

1. Aliphatic Amines

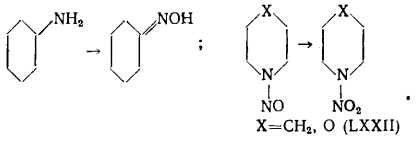
Tertiary aliphatic and cycloaliphatic amines are converted by hydroperoxides in the presence of vanadium, molybdenum, and titanium compounds into 75–80% yields of *N*-oxides [84]. *N*-Oxidation goes smoothly with bis-hydroxyethylamine and morpholine derivatives



The influence of the catalyst and of the solvent on the completeness of conversion of amines has been investigated with the oxidation of tributylamine, triethylamine, and dimethylaminoethanol by t-butyl and cumenyl hydroperoxides as examples [85]. The best catalysts are vanadium and molybdenum compounds, tungsten and niobium compounds are less active, chromium salts exhibit little activity, and cobalt, manganese, and iron salts are almost inactive. It is noteworthy that the latter completely decompose the hydroperoxide, but the yield of *N*-oxides is only 3–10%.

The oxidation of tertiary amines is less demanding on the choice of solvent. Thus in the presence of vanadium compounds high (84–96%) yields of *N*-oxides were obtained by using t-butyl alcohol, methanol, oxolan, ether, and acetone as solvents.

According to the patent literature [86] primary amines are converted by hydroperoxides, in the presence of molybdenum, vanadium, and titanium, into ketoximes, the most satisfactory results being obtained with cyclohexylamine:



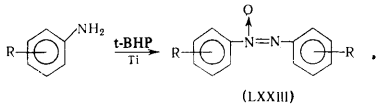
X=CH_2, O (LXXII)

The reaction of cyclohexylamine with ethylbenzene and t-butyl hydroperoxides obeyed a second-order rate equation [87]; oxidation to the ketoxime took place with high yields in the presence of titanium, vanadium, molybdenum, and tungsten compounds.

The interesting potentialities of the hydroperoxide method are demonstrated by the recently reported [45,88] examples of the conversion of nitrosamines into nitramines. In particular, nitramines (LXXII) have been obtained by the action of t-pentyl hydroperoxide on *N*-nitroso-morpholine and -piperidine in the presence of molybdenum pentachloride.

2. Aromatic Amines

Depending on the dosage of the oxidant, primary aromatic amines can be converted into azoxy-compounds or nitro-derivatives. In the presence of titanium compounds aniline, *o*- and *p*-toluidines, and *m*-nitroaniline are converted by t-butyl hydroperoxide almost quantitatively [89] into the corresponding azoxy-compounds (LXXIII):



(LXXIII)

p-Chloro-, 2,4,6-tribromo-, and *o*- and *p*-nitroanilines give unidentified products under the same conditions.

Kinetic investigation of the oxidation of *para*- and *meta*-substituted anilines to nitrobenzenes has shown [90] that the best catalysts are vanadium compounds, molybdenum being less active, and tungsten and cobalt salts completely inactive. Under optimum conditions (with t-butyl hydroperoxide and vanadyl trisacetylacetonate) the rates of oxidation of the anilines correlate well with the Hammett σ-constants and the Brown–Okamoto σ^*-constants, the values found for the ρ-constant being respectively -1.63 and -1.42. It is significant that a value of ρ of the same order (-1.86) was found for the oxidation of substituted anilines by peracetic acid [91]. The reaction mechanism in Scheme 2 has been suggested [90].

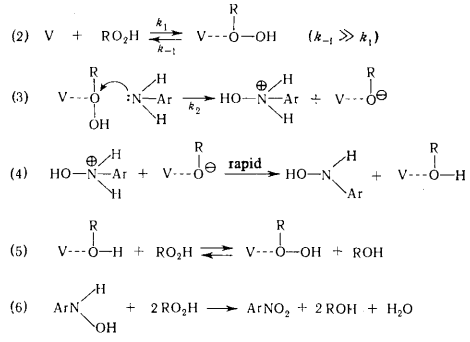
The oxidation of secondary aromatic amines has been investigated with cobalt salts as catalyst. Under these conditions the oxidant is $RO_2^{\cdot}$, which makes such reactions fundamentally different from ionic oxidation [92,93].

3. *N*-Oxidation of Aromatic Nitrogen Heterocycles

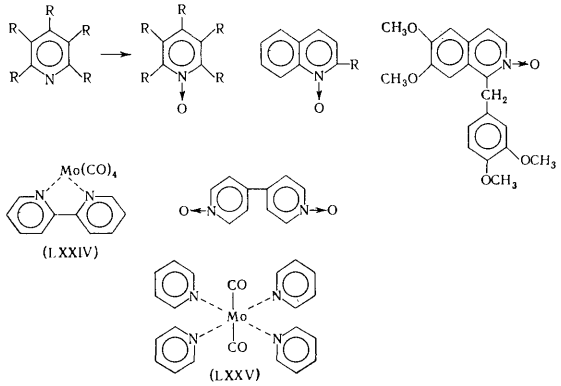
The oxidation of diverse compounds of this class has been investigated [38,45,88,94]. Almost quantitative *N*-oxidation is possible with pyridines containing one to five substituents, including such difficultly oxidisable compounds as 3,5-dibromopyridines and acetamidopyridines. The reaction is conducted in benzene solution in the presence of t-pentyl hydroperoxide with molybdenum pentachloride or hexacarbonylmolybdenum. The advantages of the proposed method can be demonstrated by the oxidation of acridine, which is converted quantitatively into the *N*-oxide after only 2 h, whereas perbenzoic acid gives merely 50% conversion after several days. Derivatives of quinoline, isoquinoline (papaverine), and naphthoquinoline are oxidised very smoothly. The possibility of obtaining the dioxides in at least 85% yield in a single stage has been shown for the oxidation of 4, 4′-bipyridyl, 2,3,5,6-tetramethylpyrazine, and phenazine.

Scheme 2

(1) Activation of catalyst (rapid)



2,2′-Bipyridyl, 1,10-phenanthroline, and 8-hydroxyquinoline stand apart in being completely unoxidised. The catalyst is firmly bound by these reactants, and does not undergo the complex formation which would activate the hydroperoxide. An investigation was therefore made of the dependence of the rate of oxidation of alkenes and pyridine on the strength of binding of the molybdenum, by conducting oxidation in the presence of complexes hexacarbonylmolybdenum, tetracarbonylbipyridylmolybdenum (LXXIV), and dicarbonyldibipyridylmolybdenum (LXXV). The catalytic activity of molybdenum dropped sharply in this sequence: whereas (LXXIV) still had a catalytic effect, the complex (LXXV) was completely inactive. It is readily seen that substituting four coordination positions with such an active ligand as 2,2′-bipyridyl prevents complex formation either with the hydroperoxide or with the substrate.

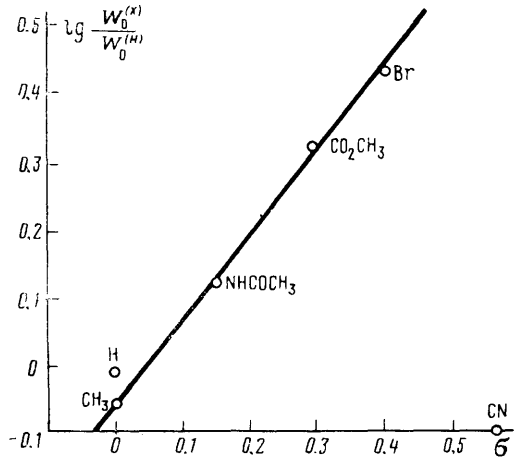


(LXXIV)

(LXXV)

Several quantitative characteristics have been obtained for the *N*-oxidation of pyridine and its 3-substituted derivatives by t-pentyl hydroperoxide in the presence of

molybdenum pentachloride [95]. In particular, it has been established that the reaction is first order with respect to substrate and hydroperoxide on conversion of up to 20% of the former. The activation energies of the oxidation of pyridine and methyl pyridine-3-carboxylate over the range 40–80°C were respectively 9.1 ± 0.2 and 7.7 ± 0.2 kcal mole^{-1}.

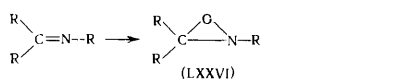


Dependence of rate of oxidation of substituted pyridines on the σ-constants.

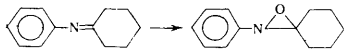
The dependence of the rate of reaction of 3-substituted derivatives on the σ-constant was very characteristic. The diagram shows that the rate increases with decrease in the electron density on the reaction centre (series constant $\rho = +1.2$). 3-Cyanopyridine is out of line with the general sequence, and has the lowest rate of oxidation. This was attributed to enhanced complexing activity of the nitrile group, resulting in blocking of the catalyst.

4. Synthesis of Oxaziridines

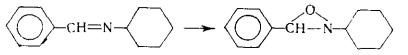
Oxaziridines are formed in yields of 40–90% when azomethines are oxidised with peroxy-acids [96]. It has recently been shown that these interesting compounds can be obtained by oxidising azomethines with t-pentyl hydroperoxide in the presence of molybdenum compounds [38,45,88]. Azines obtained from aliphatic aldehydes or ketones and amines react especially easily. Reaction goes very smoothly to give at least 80% yields of oxaziridines (LXXVI):



(LXXVI)



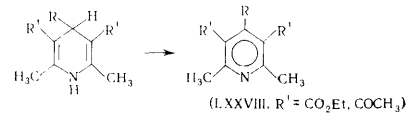
(LXXVII)



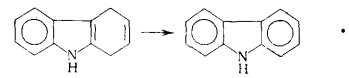
Oxaziridines (LXXVII) containing aromatic and aliphatic substituents are formed smoothly. Attempts to obtain purely aromatic oxaziridines were completely unsuccessful. Thus oxidation of benzylidenaniline is accompanied by vigorous rearrangement to benzanilide.

5. Dehydrogenation of 1,4-Dihydropyridines

One stage in the Hantzsch method for the preparation of pyridines involves the dehydrogenation of 1,4-dihydropyridines by means of various oxidising agents [97,98]. It has recently been found [99] that dehydrogenation by the action of t-pentyl hydroperoxide in the presence of molybdenum pentachloride is far more convenient. For example, diethyl 1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate is converted quantitatively into (LXXVIII):



(LXXVIII, R' = CO_2Et, $COCH_3$)
(LXXIX)

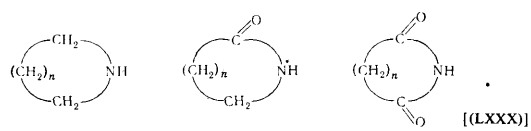


However, the conversion of 4-substituted dihydropyridines into pyridines (LXXIX) requires milder conditions, since in boiling benzene *N*-oxides are formed simultaneously. If excess of the hydroperoxide is used, *N*-oxides of the corresponding pyridines are formed in at least 80% yield in a single stage.

Dihydrocarbazole is converted quantitatively into carbazole.

6. Oxidation of Cyclic Amines to Imides

Interesting new potentialities for hydroperoxide oxidation are revealed by recent publications. It has been shown in particular that piperidine can be converted into 2-oxopiperidine [100], and caprolactam, 2-oxopiperidine, and 2-oxopyrrolidine are oxidised by t-butyl hydroperoxide to the corresponding imides [101] (LXXX)



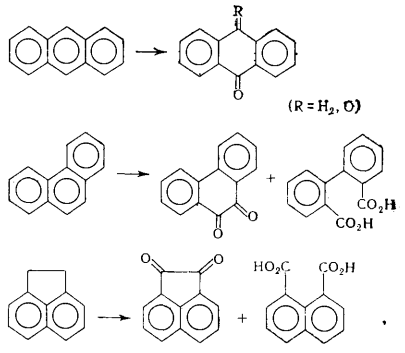
[(LXXX)]

The reactions are catalysed by bivalent and tervalent manganese salts. The yields of the imides are 65–85%, which confers preparative value on the method.

VI. OXIDATION OF FUSED AROMATIC HYDROCARBONS

Anthracene, phenanthrene, and acenaphthene can be oxidised by means of t-pentyl hydroperoxide in the presence of molybdenum pentachloride [102]. Anthracene is converted into a mixture of anthrone and anthraquinone, and phenanthrene and acenaphthene give phenanthraquinone

and acenaphthenequinone together with diphenic and naphthalic acids:

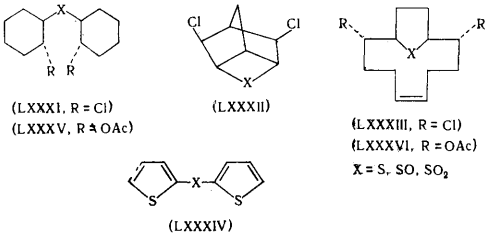


Thus the reaction involves rupture of a carbon–carbon bond. Up to 90% conversion of the hydrocarbons can be achieved by using excess of hydroperoxide. If vanadium compounds are used as catalysts, the same oxidation products are formed, but conversion of the initial compounds does not exceed 25%.

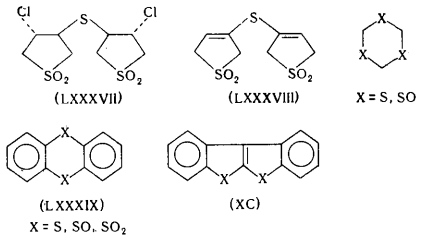
VII. OXIDATION OF ORGANOSULPHUR COMPOUNDS

Inorganic oxidising agents and peroxy-acids are generally employed to oxidise a sulphur atom in an organic compound [103,104]. The reaction between a sulphide and a hydroperoxide is very slow in the absence of a catalyst: for example, cyclohexyl methyl sulphide is converted into the sulphoxide by the action of t-butyl hydroperoxide at 60°C over a period of 64 h. [105] Some years later it was shown that aliphatic sulphides could be oxidised quantitatively to the sulphones by the action of hydroperoxide in the presence of molybdenum acetylacetonate [106]. A process of oxidation of sulphides to sulphoxides and sulphones by the action of hydroperoxides in the presence of metals of Groups IV and VII has been patented, and the partial and complete oxidation of dialkyl (diphenyl) sulphides has been described [107].

The hydroperoxide oxidation of organosulphur compounds has been most fully investigated [28,108,109]. The new method is applicable generally, since it can be used to oxidise organosulphur compounds of diverse structure. Its chief merit is extraordinarily high selectivity, not possible with the usual oxidising agents. The high rate of oxidation and the preparative simplicity are noteworthy. Hydroperoxide oxidation combines mildness of action, permitting the oxidation of compounds which undergo changes in the presence of such a reagent as hydrogen peroxide, with strong oxidising power, allowing the oxidation of sulphides and aromatic sulphur heterocycles that do not react with other oxidants. For example, the dichlorinated sulphides (LXXXI)–(LXXXIII), whose chlorine atoms are extremely labile, and dithienyl sulphide (LXXXIV) give very low yields of sulphoxides and sulphones when treated with hydrogen peroxide, whereas oxidation with t-pentyl hydroperoxide and molybdenum pentachloride in benzene solution produces almost quantitative yields of the oxidised products. The introduction of two acetoxy-groups, as in the sulphides (LXXXV) and (LXXXVI), almost completely prevents oxidation by hydrogen peroxide by shielding the sulphur atom, but high yields of sulphoxides and sulphones were obtained by means of the above hydroperoxide and catalyst.



The advantages of hydroperoxide oxidation are clearly evident from experiments on the sulphides (LXXXVII) and (LXXXVIII). Oxidation of the former with hydrogen peroxide gives a mixture of the sulphoxide and the sulphone, whereas the latter remains completely unoxidised [110]. However, the Reviewers have been able to obtain sulphoxides and sulphones in at least 90–95% yield by the action of t-pentyl or cumenyl hydroperoxide in the presence of molybdenum pentachloride. The possibility of precise control of the degree of oxidation by measuring out the oxidant has been shown with trithian as example, which is converted quantitatively into mono-, di-, and tri-sulphoxides, as well as with thianthren and 3,4,5,10-tetramethylthianthren (LXXXIX), which are converted respectively into mono- and di-sulphoxides, sulphoxidosulphones, and disulphones. Similarly, benzothiopheno[2,3-*b*]benzothiophen (XC) is converted quantitatively into the monosulphoxide and the mono- and di-sulphones; the disulphone could not be obtained by the action of hydrogen peroxide [111].

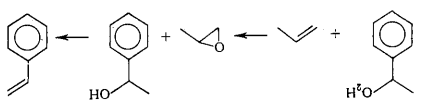


The hydroperoxide method has been applied to the selective oxidation of organosulphur compounds such as dicyclohexyl sulphide, thiadecalin, 13-thiabicyclo[8,2,1]-tridecane, benzothiophen, phenoxathi-in, phenazine, etc.

VIII. POSSIBLE INDUSTRIAL APPLICATIONS OF METAL-CATALYSED HYDROPEROXIDE OXIDATION

The development of processes for the conversion of alkenes originating from the petroleum industry into oxygen-containing compounds—oxides, alcohols, ketones, etc.—is one of the main tasks of petroleum chemistry. From this naturally follows the interest that has been evinced in the hydroperoxide epoxidation of alkenes.

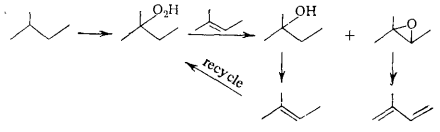
Publication of the firm Halcon International Inc. patents [112–117] on the simultaneous production of methyloxiran and styrene clearly revealed the potentiality of the new method. This process is based on the reactions



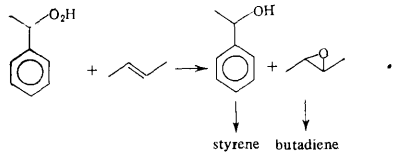
It may compete with the classical method of obtaining styrene by the dehydrogenation of ethylbenzene. A recent report on the starting-up of a plant based on the "Halcon process" states [118] that technical difficulties have been successfully overcome. Information on the production and purification of ethylbenzene hydroperoxide and on the choice of optimum conditions for oxidation will be found in patents [119-127]. The use of cumenyl hydroperoxide enables methyloxiran and α-methylstyrene to be produced together [128,129]. An interesting route has been suggested [50] for the simultaneous production of methacrylic esters and methyloxiran.

The development of improved and economic processes for obtaining isoprene is a most important task of the monomer industry. A process based on isopentane hydroperoxide is undoubtedly of interest in this connection [130-134]; its principle will be clear from Scheme 3.

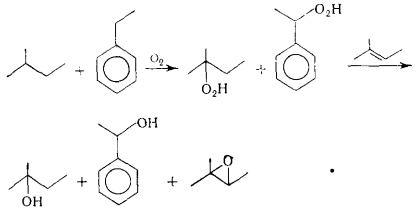
Scheme 3



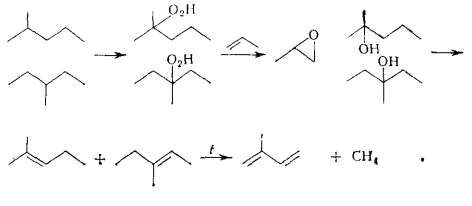
Among processes for the combined production of styrene and dienes—butadiene and isoprene—the first involved oxidation of but-2-ene by ethylbenzene hydroperoxide followed by appropriate reactions [135]:



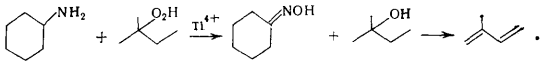
Oxidation of a mixture of isopentane and ethylbenzene is claimed [136] to yield the corresponding hydroperoxides, which are then used to oxidise isopentene to the oxide, after which the reactions are similar to those described above:



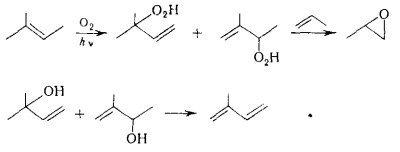
A noteworthy combined process for obtaining isoprene and methyloxiran from 2- and 3-methylpentane hydroperoxides yields tertiary alcohols, which crack to form isoprene [137]:



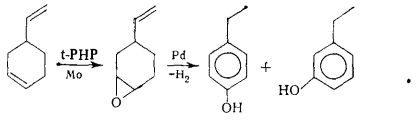
The production of isoprene can be combined with that of cyclohexanone oxime, which is formed by oxidising cyclohexylamine with hydroperoxides in the presence of titanium salts [137,138]:



An extremely interesting process for obtaining isoprene and methyloxiran is based on unsaturated hydroperoxides formed by the photosensitised oxidation of isopentene [139]:

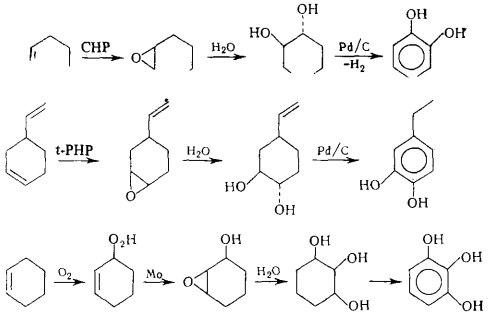


It has been proposed to use hydroperoxide epoxidation as a stage in the production of phenols. In particular, a mixture of *m*- and *p*-ethylphenols is obtained by the scheme [140]

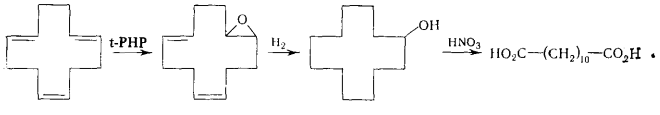


The essential nature of methods developed for obtaining catechol [141,142], ethylcatechol [143], and pyrogallol [144] will be clear from Scheme 4.

Scheme 4



A suggested method for obtaining dodecanedioic acid involves the stages [145]



The application of hydroperoxide epoxidation to the production of various oxygen-containing compounds is considered in periodical communications [146-152] and in patents [153-157].

While the Review was being prepared for press several publications have appeared on the kinetics and the mechanism of hydroperoxide epoxidation [158-163]. Papers clearly showing for the first time that the reaction is catalysed by complexes of sexivalent molybdenum are especially interesting [158,159]. The stereochemistry of oxidation has been examined [164-166].

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Effect of a Strained Double Bond on the Behaviour of Hydrocarbons Towards Oxygen

V.V.Voronenkov

The reasons for strain in a double bond are considered, and the effect of the stress on the behaviour of hydrocarbons in liquid-phase oxidation and in oxidative polymerisation is discussed. The list of references contains 39 items.

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III. Oxidation of a double bond with "torsional stress" 334
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I. INTRODUCTION

The oxidation of hydrocarbons by molecular oxygen is currently attracting the attention of many research workers. The literature on this process [1–4] indicates that the scientific problems of oxidation are indissolubly linked with general aspects of structure and reactivity. I have therefore examined the effect of a strained double bond on the behaviour of hydrocarbons in reactions with oxygen.

All substituents adjacent to a double bond are in the same plane as the alkene group and the angle [5]

is normally taken to be 120°. Departure from this angle requires the consumption of energy: i.e. it increases the internal energy of the system. Thus a strained double bond is understood to be one which, in contrast to the "ideal" geometry, is subject to strong angular distortions with enhanced energy of the system. Such systems were discussed comprehensively in a review by Zefirov and Sokolov [6]. However, they did not consider the effect of a strained double bond on the reactivity of hydrocarbons towards oxygen, a gap to be filled in the present Review.

II. OXIDATION OF A DOUBLE BOND WITH "CISOID REPULSIVE STRESS"

Hecht and Victor [7] found by proton magnetic resonance spectroscopy that rotation of the methyl groups in *cis*-but-2-ene was hindered compared with that in the *trans*-isomer. They also proved that the skew conformation of *cis*-but-2-ene, obtained from the form with the methyl protons shielding the double bond, was energetically the most favourable. Such a conformation exhibits fairly strong overlapping of the van der Waals spheres (Fig. 1), leading into an increase in the angle θ. It must be borne in mind that the deformation of this angle between the bonds is not localised, but distributed over the other angles, as a result of which the energy of the system as a whole is minimised. This involves deformation of the remaining angles and an increase in the strain in the double bond ("cisoid repulsive stress").

The strain in a double bond can be assessed experimentally from thermodynamic data by comparing the negative heats of hydrogenation of the alkenes. Table 1 shows that increase in the volume of *cis*-alkyl groups in an alkene produces an increase in the negative heat of hydrogenation, which corresponds to greater stress in the >C=C< bond, and so to greater deviation of the valency angle θ, which becomes 136° in *cis*-di-t-butylethylene [*cis*-2,2,5,5-tetramethylhex-3-ene]. The main consequence of such stress in the double bond is enhanced reactivity.

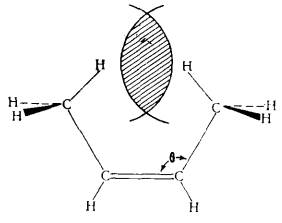


Figure 1. Diagram of overlapping of van der Waals spheres in *cis*-but-2-ene (from proton magnetic resonance data [7]) with distances (Å) C=C 1.38, C–C 1.54, and C–H 1.06 and angles CCC 120° and CCH 109.5°.

Table 1. Negative heats of hydrogenation of isomeric *cis*- and *trans*-alkenes [6].

Alkene	$-\Delta H_{hydr}$, kcal mole^{-1}	Alkene	$-\Delta H_{hydr}$, kcal mole^{-1}
cis-But-2-ene	28.57	*cis*-Methyl-t-butylethylene	30.8
trans-But-2-ene	27.62	*trans*-Methyl-t-butylethylene	26.5
cis-Methylisopropylethylene	28.60	*cis*-Di-t-butylethylene	36.2
trans-Methylisopropylethylene	27.76	*trans*-Di-t-butylethylene	26.87

In the epoxidation of alkenes by hydroperoxides in the presence of a molybdenum catalyst, represented by the general scheme

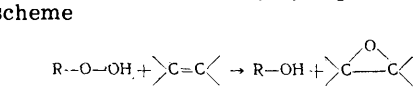


Table 2. Reactivities of isomeric butenes (4.0 M) in epoxidation on a molybdenum catalyst [8] (0.0001 M) at 50°C.

Alkene	Rate constant, $M^{-1}\ s^{-1}$	Relative rate
But-1-ene	$0.076 \cdot 10^{-3}$	1.00
trans-But-2-ene	$1.08 \cdot 10^{-3}$	14.2
cis-But-2-ene	$2.74 \cdot 10^{-3}$	36.0

for example, the reactivity of *cis*-but-2-ene is considerably greater than that of the *trans*-isomer (Table 2). A similar rule is observed in the epoxidation of cycloalkenes: those having a strained double bond (norbornene, cyclopentene) are epoxidised far more readily than are cycloalkenes not containing a strained double bond (cyclohexene) [9]. *cis*-Polybutadiene is oxidised by oxygen more vigorously than is *trans*-polybutadiene [10].

III. OXIDATION OF A DOUBLE BOND WITH "TORSIONAL STRESS"

"Torsional or twisting stress" in a double bond results from a fragment of the molecule turning about the double bond (Fig. 2), which reduces the degree of overlap of the p_z atomic orbitals. Quantum-mechanical calculations show that the energy of a π-bond is greatest with maximum overlap of these orbitals, which occurs when they lie in the same plane. Deflection of the axes of the orbitals from coplanarity decreases their degree of overlap, ultimately with the appearance of a biradical triplet state.

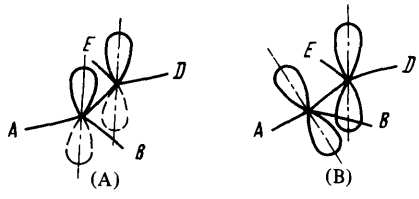
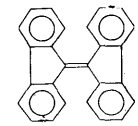


Figure 2. Diagram of the overlap of p_z orbitals in model of: A) coplanar state; B) strained state.

The graph shows (Fig. 3) how the energies of the ground level N, the first triplet level T, and an excited level V in ethylene vary with mutual rotation of the moieties of the molecule [11,39]. With increase in the angle of deflection the $N-V$ transitions require less energy: i.e. excitation occurs at longer wavelengths, and at an angle of 90° the triplet state now becomes energetically more favourable than the singlet state.

One mode of homolysis of an ethylenic bond, i.e. of mutual approach of ground and triplet levels N and T, is a decrease in the degree of overlap of the p_z atomic orbitals of the π-bond (Fig. 2). Such a state arises in ethylenic bonds with "torsional stress", e.g. in 9,9′-bifluorenylidene [12]



(I)

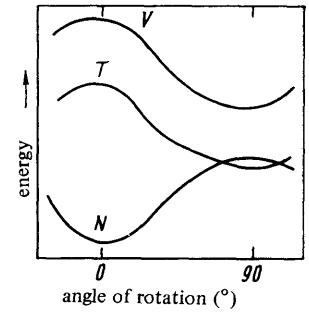
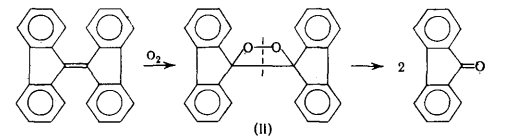
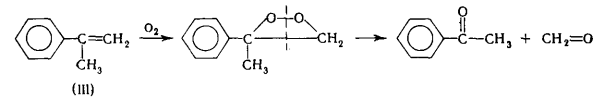


Figure 3. Variation of ground level N, first triplet level T, and excited level V of ethylene during rotation about the double bond [11].

Here the double bond is strained because left-hand and right-hand moieties of the molecules are turned apart by the repulsion of the non-bonded *peri*-hydrogen atoms. This leads to decreased overlap of the p_z atomic orbitals, i.e. to diminished coupling (overlapping) of the electrons forming π-bond and to an increased degree of homolysis of this bond. Such bonds exhibit an enhanced tendency to undergo homolytic (radical) reactions. This is supported by the fact that 9,9′-bifluorenylidene readily terminates reaction chains in the oxidation of benzaldehyde, thereby being oxidised to fluorenone. It is also extremely readily oxidised to fluorenone by atmospheric oxygen in ethereal or alcoholic solution. The sensitised photochemical oxidation of 9,9′-bifluorenylidene occurs highly selectively to give a 91% yield of fluorenone [13]. The oxidation probably involves intermediate formation of 1,2-dioxetans:

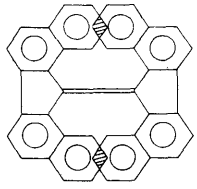


Oxidation of the double bond in α-methylstyrene obviously has the same mechanism:



It is interesting that the rate of oxidation of the double bond in bifluorenylidene exceeds that in *trans*-4-methylpent-2-ene—a compound from whose double bond torsional stress is completely absent—by a factor of 720. [13]

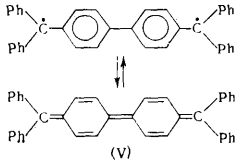
Homolytic reactions are still more characteristic of the double bond in bisdibenzo[*a*,*i*]fluorenylidene



(IV)

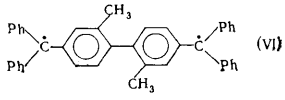
This hydrocarbon inhibits the autoxidation of certain organic compounds, in particular benzaldehyde, slows down the polymerisation of styrene, and in toluene solution readily reacts with oxygen when exposed to ultraviolet radiation [14].

Among compounds with torsionally stressed double bonds is Chichibabin's hydrocarbon [15]



(V)

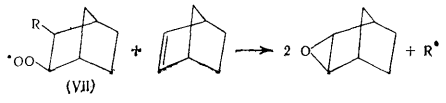
It adds oxygen fairly easily to form a peroxide, but if methyl groups are introduced into the *oo'*-positions of the biphenyl system the product



(VI)

is oxidised still more vigorously to a peroxide [16]. Interaction of the methyl groups results in complete uncoupling of the *p*-electrons of the central π-bond in biphenyl [17].

In cycloalkenes, especially in the bicyclic compounds, e.g. norbornene and its derivatives, serious angular deformations, leading to stress in the double bond, arise from the conditions of ring closure. Zefirov and Sokolov predicted that the study of strained cycloalkenes could lead to the discovery of fundamentally new reactions [6], a forecast which has recently been fulfilled. The oxidation of norbornene and its derivatives by oxygen has shown that the t-C–H bond in them is inert [18–20]. In the presence of azoisobutyronitrile, however, oxidation is fairly vigorous. The oxidation products are not hydroperoxides—as occurs in the oxidation of cycloalkenes whose double bond is unstressed—but cyclic oxides. This was explained [20] by a mechanism in which the epoxidising agent was a peroxy-radical formed by addition of a free radical R$^{\bullet}$ to one end of the double bond and of oxygen to the other end. Such a peroxy-radical (VII) reacts with the initial compound to form two molecules of the oxide:

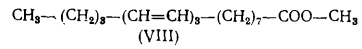


(VII)

Interaction of the radical with the strained double bond suggests that the stress makes the latter liable to radical dissociation (to become partly homolysed).

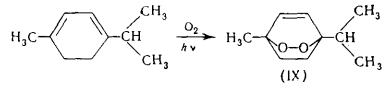
IV. EFFECT OF TENDENCY OF DOUBLE BONDS TO HOMOLYSIS ON THE REACTIVITY OF HYDROCARBONS TOWARDS OXYGEN

It will be extremely interesting to examine the oxidation of conjugated diene and polyene systems in terms of homolysis of the double bonds. These systems differ from monoalkenes and unconjugated polyenes in usually not forming hydroperoxides even when a methylene group appears at first glance to be in a position favourable for oxidation, e.g. in elaeostearic ester [21]



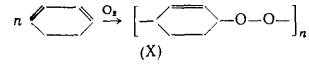
(VIII)

Instead, oxygen tends to add at the ends of a diene segment with formation of an oxygen bridge, as in transannular peroxides [22]:



(IX)

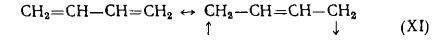
Polymeric peroxides



(X)

may also be formed [23,24]. All the above published information suggests that the interaction of alkenes and polyalkenes with oxygen is strongly dependent on the liability to homolysis of the bonds in the hydrocarbon.

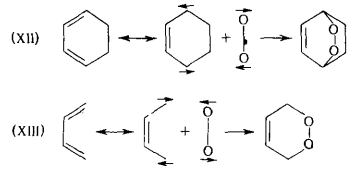
In conjugated diene systems, e.g. butadiene and cyclohexadiene, neighbouring π-bonds do not remain strictly localised, but interact with partial overlapping of the *p*-electrons of double bonds in positions 2 and 3. As a result of this interaction, the double bonds 1–2 and 3–4 become partly uncoupled (homolysed), which can be represented conventionally by



(XI)

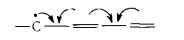
The arrows below the outer carbon atoms on the right-hand side denote single electrons, and their opposite directions indicate opposite spins [25,26]. Thus the uncoupling of the electrons at the ends of a diene system leads to weakening of the terminal bonds, which increases their activity in radical reactions. The right-hand formula obviously corresponds to an excited state of the butadiene molecule.

According to resonance theory, individual resonant structures do not correspond to physically real molecular states [27]. Recognition of the partial uncoupling of electrons in double bonds leads to the conviction that the symbols used by resonance theory can probably represent the excited (real) state of a molecule and—what is most important—predict the course of chemical (homolytic) reactions. This conclusion is confirmed by known oxidations of hydrocarbons, e.g. butadiene, cyclohexadiene, cyclohexene, and elaeostearic ester. Cyclohexadiene (XII) and butadiene (XIII) give with oxygen cyclic peroxides, which can be represented by the scheme



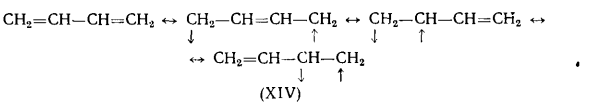
The right-hand formulae for the hydrocarbons have greater energy than the usual formulae on the left. With a planar arrangement of atoms in the molecule the two right-hand formulae have a different distribution of p-electrons and approach a triplet biradical state in which the ethylenic carbon atoms are no longer so double-bonded in character.

The concept of the uncoupling of electrons of a π-bond under the influence of a free electron in an allyl radical was put forward long ago in the early papers by Burton and Ingold[28]. In particular, they regarded stabilisation of a radical as involving interaction of an unpaired electron with the electron pair of a neighbouring π-bond, leading to partial uncoupling of the latter and a redistribution of electrons:



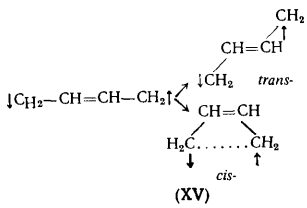
Ingold writes[29]: "In this paper, the main conclusions of which are partly applicable to the whole theory of organic chemistry, reference was first made to the relation between mesomerism and the uncertainty principle and to the fact that the motive force distributing electrons along a conjugated chain is of quantum origin".

The concept of partial uncoupling of electrons of a π-bond suggests that in an excited state butadiene may exist in the forms



(XIV)

The 2–3 bond obviously has one-third double-bond character, so that free rotation is unlikely about this bond. Separate existence of *cis*- and *trans*-forms of butadiene is therefore possible:

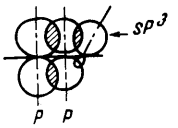


(XV)

Since the outer groups approach very closely in the *cis*-system, a homocomplex may be formed. The increased proportion of the *cis*-form of butadiene with rise in temperature (e.g. in diene synthesis) probably results not from rotational isomerism but from an increase in the statistical weight of the excited *cis*-form.

The above facts suggest that the liability of double bonds in a molecule to homolytic breakdown may well be as important in the oxidation of hydrocarbons as are the properties of the radical. Thus from a comparison of the interaction of peroxy-radicals of α-methylstyrene, styrene, and methyl methacrylate with monomers Mayo concluded[30] that the oxidation of vinyl monomers is governed mainly by the activity of their double bond.

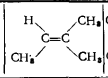
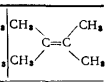
It follows from the above considerations that the hyperconjugation of α-CH bonds in alkenes and alkylated aromatic hydrocarbons can also be explained by their tendency to homolysis (partial uncoupling of the electrons of the α-CH bond). On certain postulates the interaction of an α-CH bond with the π-electrons of a double bond, e.g. in propene, is analogous to the interaction of π-electrons in a conjugated system. This can be represented[31]



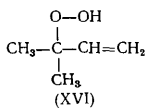
Here the hybrid sp^3 orbitals overlap the p_z orbitals of the double bond. Such interaction would probably result in partial uncoupling of the α-CH bond, its partial homolysis. The tendency to such homolysis will be most effective when the axis of the α-CH bond and the axes of the p-electrons are completely or nearly parallel, i.e. when the double bond is not weakened by steric factors. A partly uncoupled (homolysed) α-CH bond has far greater electron affinity for a peroxy-radical than has the unhomolysed bond. Attack by such a radical in the autoxidation of alkenes is therefore directed at an α-CH bond. In monoalkenes the double bond interacts with the α-CH bonds and homolyses them.

In the hyperconjugation effect the interaction of alkyl group and double bond is a reciprocal process. For example, a consequence of replacing an ethyl group in propane by vinyl is that the methyl group in propene reacts considerably more readily with oxygen than does a methyl group in propane. Replacing a hydrogen atom in ethylene by a methyl group makes the double bond in propene more susceptible to epoxidation than is the double bond in ethylene. Thus the relative rates of epoxidation of ethylene, propene, isobutene, trimethylethylene [2-methylbut-2-ene], and tetramethylethylene [2,3-dimethylbut-2-ene] are respectively 1, 21, 30, 5600, and 6000.[32] This is paralleled by a fall in the ionisation potential (Table 3): increase in the number of methyl groups in a molecule leads to a fall in the ionisation potential and an increase in the rate of epoxidation.

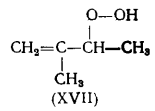
Table 3. Ionisation potentials of alkenes[33].

Alkene	$CH_2=CH_2$	$CH_2=CH-CH_3$	$CH_2=C(CH_3)_2$		
Ionisation potential, eV	10.62	9.84	9.35	8.85	8.45

The low-temperature autoxidation of hydrocarbons such as tri- and tetra-methylethylenes involves intermediate formation of an allyl radical. Examination by proton magnetic resonance spectroscopy of the products of the low-temperature oxidation of trimethylethylene has established the formation of two hydroperoxides—tertiary and secondary[34]

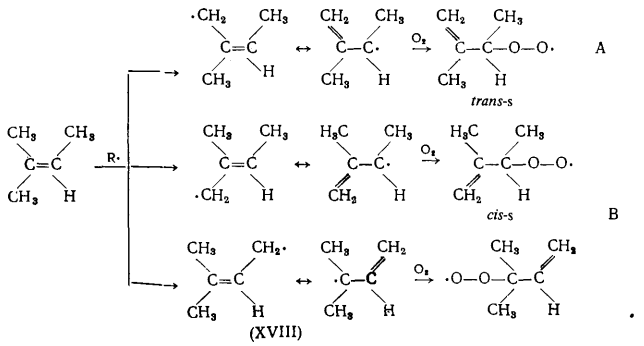


(XVI)



(XVII)

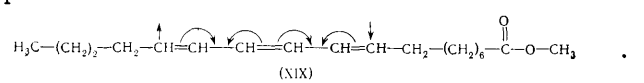
This can be explained in terms of resonance in the hydrocarbon free radicals of the isoalkene in the forms (XVIII) A and B



(XVIII)

All the free radicals indicated are equally likely to react with oxygen, but the probability of forming primary hydroperoxides is small because of the short lifetime of a primary allyl hydrocarbon radical. The more stable tertiary and secondary radicals are formed from the primary radicals. Since the rate of radical abstraction of the hydrogen atom is the same from all three methyl groups in trimethylethylene, the number of resonance structures formed under otherwise similar conditions is twice as great for a secondary radical (*cis*-s, *trans*-s) as for a tertiary radical. Therefore the statistical probability of involvement in reaction with oxygen is considerably greater for a secondary radical (form A) than for a tertiary radical (form B). This evidently explains why the quantity of secondary hydroperoxide formed is double the quantity of the tertiary hydroperoxide. Thus in this example the structure and the proportions of the hydroperoxides are governed solely by the number of resonance structures of the hydrocarbon free radicals.

If a system of conjugated double bonds is present, interaction of the π-electrons will evidently be stronger than that between double and α-CH bonds. In diene systems, therefore, the π-bonds—not the α-CH bonds—are homolysed (uncoupled) first. An example is the oxidation of cyclohexadiene. Elaeostearic esters are oxidised similarly, when uncoupling of the electrons may be represented



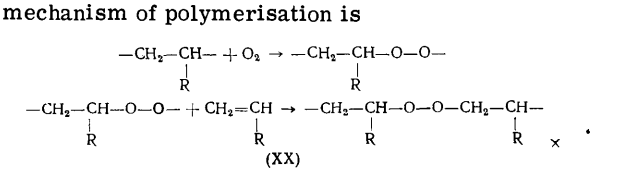
(XIX)

Radical unsaturation appears predominantly at the ends of the diene system, at which the action of oxygen is directed.

It is interesting that the addition of phenyl rings at the ends of a double bond increases the tendency to homolysis and accelerates oxidation of the double bond. For example, the rates of oxidation of the double bond by oxygen with formation of polyperoxides increase in the sequence [35]

styrene < α-methylstyrene < 1,1-diphenylethylene.

The mechanism of polymerisation is



(XX)

Table 4 lists kinetic data on the radical polymerisation of vinyl acetate with the above monomers [36]. This process is interesting because the same radical is interacting with the double bond in monomers having different structures.

The difference in reactivity of the above monomers therefore represents primarily a difference in the electronic nature of their double bond. Weakening of the double bond is greater in 1,1-diphenylethylene than in styrene, probably an effect of the two phenyl rings, which exert a stronger homolysing action on the π-bond. 1,1-Diphenylethylene is a structural analogue of benzophenone, in which the carbonyl π-bond passes considerably more readily into the triplet (biradical) state than does the corresponding bond in benzaldehyde [37]. Thus homolysis of the π-bond in hydrocarbons is promoted by steric factors (torsional or angular stress) and electronic factors (effect of non-polar substituents adjacent to double bonds capable of $\sigma-\pi$ or $\pi-\pi$ conjugation).

Table 4. Stoichiometric coefficient* of vinyl monomers in the polymerisation of vinyl acetate at 50°C. [36]

Monomer	μ_{theor}	μ_{exp}	$\frac{\mu_{exp}}{\mu_{theor}}$
Styrene	2.0	0.065	0.032
α-Methylstyrene	2.0	0.65	0.32
1,1-Diphenylethylene	2.0	1.77	0.88

*μ = stoichiometric coefficient in the equation $t_i = \mu z_0/w_1$, where t_i is the duration of the induction period, z_0 the initial inhibitor concentration, and w_1 the rate of initiation.

The increase in the polarity of the ethylenic bond may even produce an ambipolar ion $\overset{+}{\text{C}}-\overline{\text{C}}$, in which rotation about the central bond does not result in a decrease in the overlap integral between the p-electrons, since they are concentrated in the region of a single carbon atom. This situation diminishes the effect of the double bond on the α-CH bonds. It now becomes clear why, for example, the rate of autoxidation of 2-methylpent-1-ene is one-tenth of that of 2-methylpent-2-ene [38]: the double bond is polarised only in the former hydrocarbon.

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Advances in the Synthesis and Investigation of Organofluorine Compounds

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Modern data concerning the wide variety of the physical and chemical properties of organofluorine compounds are reviewed. The studies in recent years, carried out using non-empirical quantum-mechanical calculations, photoelectronic spectroscopy, ^{19}F and ^{13}C NMR, as well as other latest research techniques, have introduced a number of refinements into ideas on the effect of fluorine atoms on the properties of both stable molecules and reaction intermediates.
The principal fields of practical application of organofluorine compounds are also examined. New data on the methods of introducing fluorine into organic molecules are presented in the concluding section.
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I. THE SCOPE OF MODERN FLUORINE CHEMISTRY

Classical organic chemistry constituted an elegant system the fundamental components of which were hydrocarbons—not only as the basis for the classification of any compound containing carbon–carbon bonds but also as a class of substances from which all these compounds can be synthesised by an appropriate sequence of experimental procedures.

The problem of the possibility of another non-hydrocarbon system, comparable in its chemical scope to the classical system, evidently arose simultaneously with organic chemistry. In the search for an answer to this problem twentieth century chemists undertook comprehensive studies on compounds in which both or at least one of the fundamental organogenic elements (carbon and hydrogen) is fully substituted by another element.

Saturated fluorocarbons, the study of which began as late as the 1930s, initially attracted attention by their complete chemical inertness. In combination with excellent thermodynamic characteristics, this property made Freons—derivatives of methane or ethane substituted by fluorine and chlorine atoms—ideal cooling agents in refrigeration engineering.

The set of properties of saturated fluorocarbons and fluorinated polymers made them essential materials for the most important branches of industry which arose in the 1940s—atomic and aerospace engineering. Their resistance to the action of the most powerful oxidising agents permitted the employment of fluorocarbons as lubricants for apparatus in contact with uranium hexafluoride or rocket fuel oxidants.

Even a very powerful oxidising agent such as atomic fluorine reacts only slightly with CF_4 (exchange with ^{18}F)[1]; on the other hand, when perfluorocycloalkanes, for example cyclo-C_4F_8, react with ^{18}F, the dissociation of C–C bonds is twice as likely as that of C–F bonds[2]. As a result of the accumulation of C–F bonds in fluoropolymer molecules, they are not only resistant to chemical action (Teflon is not acted upon either by aqua regia or concentrated alkali, which dissolve even platinum) but also have a low coefficient of friction. This property is associated with the very weak intermolecular interactions characteristic of fluorocarbons. Thus the boiling points of the lowest saturated fluorocarbons are close to those of the corresponding hydrocarbons, but, starting with the C_5 compounds, normal fluorocarbons boil at lower temperatures than hydrocarbons. On the other hand, when account is taken of the high molecular weight of fluorocarbons, it is found that the curve relating their boiling points to molecular weight is close to the corresponding curve for the inert gases[3].

In consequence of their high volatility in combination with chemical inertness, fluorocarbons have found extensive applications as components of aerosol compositions; their high vapour density makes them excellent fire-extinguishing agents.

Owing to the lack of polar interactions of the long fluorocarbon chains with the surrounding medium, fluorocarbon derivatives containing ionogenic groups (carboxylic and sulphonic acids, quaternary ammonium salts[4]) proved to be most valuable surface-active substances. Thus the addition of 0.35% of perfluorocaprylic acid lowers the surface tension of water to 15.3 dyn cm^{-1} (cf. the usual carboxylic acids for which the decrease is at most to 24 dyn cm^{-1}). Fluorocarbon residues interact weakly also with hydrocarbon chains. Thus successive substitution of hydrogen atoms in benzene derivatives by fluorine leads to a decrease of the solubility of alkanes in the latter (determined by gas–liquid chromatography[5]).

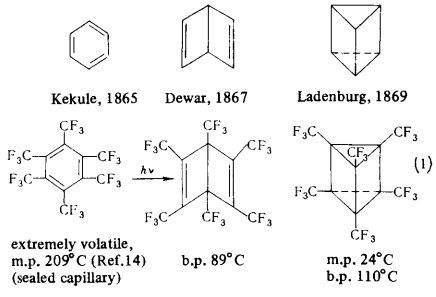
For this reason, impregnation of textiles with fluorocarbon derivatives imparts to them not only hydrophobic but also oil-repellent properties.

Their high breakdown voltage and thermal conductivity have led to the use of fluorocarbons and some of their derivatives as cooling dielectrics.

The industrial applications of fluorocarbons enumerated above (reviewed in detail elsewhere[6-11]) have led to interest in the development of convenient methods for their synthesis and in the 1940s and 1950s there was an explosive growth of the stream of empirical data on organofluorine chemistry. New facts did not always fit within the framework of ideas current at the time, which led to a tendency towards some autonomy in fluorine chemistry. However, progress in theoretical organic chemistry, which was particularly enriched by the method of investigation of electronic effects of substituents by measurements of the chemical shift of the fluorine label (see the review of Emsley and Phillips[12]) and also the adoption by many chemists working in synthetic chemistry of the

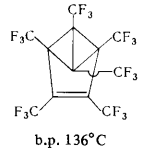
experimental achievements in fluorine chemistry made it a kind of branch of organic chemistry, a distinctive feature of which is the extreme richness of its synthetic possibilities. One may say that fluorocarbons constitute the non-hydrocarbon system which was sought by the chemists of the past, the wide variety of whose reactions surpasses the classical hydrocarbon system in certain respects.

The introduction of fluorine atoms makes it possible to isolate in a pure form structures which were regarded in classical organic chemistry as short-lived or as hypothetical reaction intermediates. Thus the introduction of six trifluoromethyl groups into the benzene ring makes it possible to isolate valence isomers corresponding to the different benzene formulae proposed in the XIXth century[13]:



(1)

The derivative corresponding to benzvalene, the existence of which had not been postulated in the XIXth century, was also isolated:



In this case the valence isomers are thermodynamically much more stable than the non-fluorinated analogues: their free energies of aromatisation are almost twice as small as for the isomers of hexamethylbenzene. The activation energy for this transformation also exceeds the value characteristic of hexamethylbenzene[15]. For comparison, we may point out that prismane C_6H_6, which was recently obtained by an elegant synthesis from benzvalene, has explosive properties[16].

Functional groups with highly oxidising properties can be introduced into fluorocarbons, i.e. it is possible to synthesise compounds whose hydrocarbon analogues are difficult to imagine: organic hypofluorites (CF_3OF)[17], superoxides (CF_3OOOCF_3)[18], derivatives of quinquevalent iodine (CF_3IF_4)[19] or halogenoperoxides (CF_3OOCl)[20].

The stabilising effect of fluorine atoms is also very marked when they are introduced into organometallic compounds. Thus the best method for the purification of fluoroalkyl derivatives of mercury[21] is distillation from concentrated sulphuric acid.

The physical properties of fluoroalkyl derivatives of metals are also sharply different from those of their hydrogen analogues. Whereas dimethylmercury is a mobile liquid with all features of a typical covalent compound, bis(trifluoromethyl)mercury is a solid (albeit volatile), which melts at 163°C in a sealed capillary; it dissolves readily in water forming conducting solutions[22].

Owing to the stabilising effect of fluorine atoms, it is possible to isolate in a pure crystalline form compounds containing a σ bond between the fluoroalkyl residue and the transition metal atom. Hydrogen-containing analogues of such compounds are frequently either unstable at room temperature or their existence as intermediates is merely postulated. Thus dehalogenation by iron pentacarbonyl[23] may involve a stage in which unstable σ derivatives of iron are formed.

On the other hand, when 1,2-dibromotetrafluoro-ethane is introduced into the reaction with $Fe(CO)_5$, the main product is an organometallic compound. Tetrafluoroethylene is isolated only on heating[24]:

$$BrCF_2CF_2Br + Fe(CO)_5 \rightarrow BrCF_2CF_2{-}Fe(CO)_4Br + CO \xrightarrow{\Delta} CF_2{=}CF_2\ (+CF_2{=}CFBr)\,. \qquad (2)$$

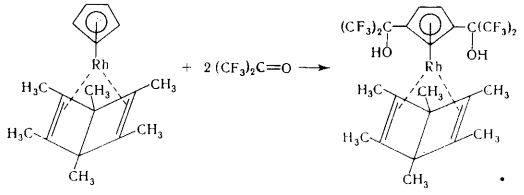
Yet another reaction in which the intermediate formation of σ compounds of transition metals was merely postulated is the synthesis of biphenyls by allowing cobalt salts to react with arylmagnesium halides. When pentafluorophenylmagnesium bromide is introduced into the reaction, the product is a blue solid—bis(pentafluorophenyl)cobalt—stable on long storage in solution. Decafluorobiphenyl is obtained only on heating this compound or on oxidising it with air[25]:

$$C_6F_5MgBr + CoBr_2 \rightarrow (C_6F_5)_2Co \xrightarrow{O_2} C_6F_5{-}C_6F_5\,. \qquad (3)$$

Many organofluorine compounds are extremely reactive. Thus the carbonyl group in fully fluorinated ketones is so electrophilic that hexafluoroacetone is "inserted" in the C–H bond of isobutene at room temperature[26]:

$$(CF_3)_2C{=}O + \begin{matrix} H_3C \\ H_3C \end{matrix}\!\!>\!C{=}CH_2 \rightarrow (CF_3)_2C(OH){-}CH_2{-}C(CH_3)_2{=}CH_2 \qquad (4)$$

or into the bond of cyclopentadiene coordinated to a rhodium atom[27]:

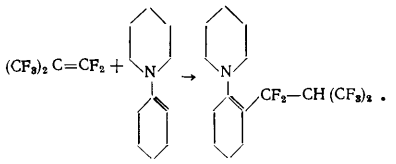


(5)

The immediate proximity of the fluorine atoms results in an extremely marked increase of the electrophilicity of carbon–carbon double bonds too. Thus octafluoroisobutene reacts at room temperature with comparatively weak nucleophilic agents such as alcohols[28]:

$$(CF_3)_2C{=}CF_2 + ROH \rightarrow (CF_3)_2CH{-}CF_2OR + (CF_3)_2C{=}CFOR \qquad (6)$$

or enamines[29]



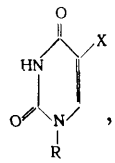
(7)

Evidently the high toxicity of octafluoroisobutene is due precisely to the ease of its reaction with nucleophilic centres and its nature is therefore analogous to that of the toxicity of many alkylating agents[30].

The physiological activity of organofluorine compounds is by no means always manifested by their toxicity. Certain fluorine-containing derivatives of ethane ("fluorotan" $CF_3CHClBr$, "inhalan" $CCl_2HCF_2OCH_3$ and its numerous analogues[31]) are valuable anaesthetics, which are almost free from side effects; fluorotan is used in paediatric surgery.

It is remarkable that the anaesthetic property of these compounds is associated with their low polarity. This property is more pronounced the greater the solubility of the substance in the non-polar lipids forming part of the membrane of the nerve cell[32].

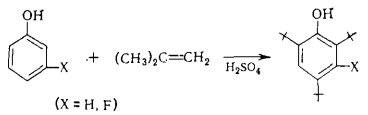
The introduction of fluorine atoms into the molecules of medicinal preparations frequently makes it possible to achieve striking results. Thus the substitution of hydrogen in the 5-position of the uracil molecule by fluorine[33] or the CF_3 group[34] leads to the formation of very effective antitumour preparations:



where X = F and R = H, , or riboside or X = CF_3

and R = riboside. Despite the fact that both preparations are antimetabolites, the mechanisms of their actions are completely different.

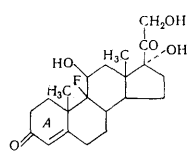
The action of 5-fluorouracil is based on the fact that the small fluorine atom leads to only a slight alteration in the geometry of the molecule, which thus retains its ability to combine the enzymes controlling its metabolic transformations. However, the latter become impossible owing to the presence of the firmly bound substituent in the 5-position. As an illustration of the low degree of steric hindrance associated with the replacement of the hydrogen atom by fluorine, one may quote an instance from the syntheses of hindered phenols: on alkylation with isobutene, three t-butyl groups can be introduced when only hydrogen or fluorine are present in the *m*-position[35]:



(X = H, F) (8)

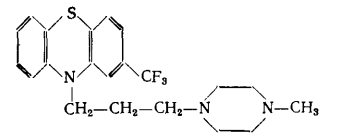
5-Trifluoromethyluridine suppresses the action of enzymes in a different way: the fluorine atoms in its molecules possess some mobility as a result of which it can alkylate the active centres of enzymes[36].

However, in the case of steroids, the slight change in molecular geometry caused by the introduction of a fluorine atom is sufficient to influence their physiological activity very significantly. Thus 9-α-fluorocortisol, whose antitumour activity exceeds that of cortisol by a factor of 7–10, differs from the latter only by the position of the *A* ring in space, which makes its molecular geometry similar to that of 6-methylprednisolone. On the other hand, the electronic defects associated with the introduction of fluorine do not play a significant role, contrary to expectation[37]:



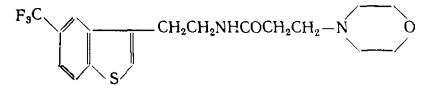
Fluorine-containing derivatives of phenothiazine and benzodiazepine are used as cyclotropic preparations.

According to polarographic data, *N*-substituted phenothiazines, including triphthazine which is used in clinical practice, form complexes with molecular oxygen.

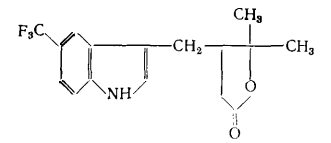


It may be that the mechanism of the action of derivatives of phenothiazine preparations consists in the formation of such complexes, which leads to a change in the energetics of cell respiration[38]. The especially high efficiency of the fluoroalkyl derivative can probably be related to the high solubility of oxygen in fluorocarbons. As a result of this property, solutions of oxygen in inert organofluorine compounds (fully fluorinated ethers, tertiary amines, and others) can find applications as substitutes for blood which, are hardly inferior to the latter in their oxygen capacity[39].

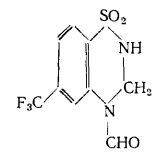
According to patent literature, fluorine-containing heterocycles can exhibit a depressive activity[40]:



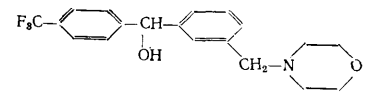
can stimulate the contraction of cardiac muscle[41]:



can reduce blood pressure[42]:



and can exhibit anti-inflammatory and antidiabetic activity[43]:



as well as diuretic[44], antimalarial,[45] and antifungal[46] activity. In addition they can have anticonvulsant properties[47], can reduce appetite[48], and can be used as sugar substitutes for diabetics[49].

The examples enumerated above, chosen from a number of patents published as late as 1972, clearly illustrate the continuous expansion of the applications of organofluorine compounds. As a result of this process, studies in the field of organofluorine chemistry have begun to develop at an ever increasing rate, the rate of growth of the number of publications in this field exceeding the average (which is also very high) for chemical literature as a whole. Thus the number of publications in 1970 on fluorine chemistry was three times greater than in 1960 and the number of new compounds described in these papers was five times greater[50]. On the other hand, the total number of chemical publications (and the compounds synthesised) doubles only every 8.3 years[51].

The available information about organofluorine compounds has been distributed in recent years among a large number of publications, many of which are difficult to obtain. Thus in 1969–1970 90% of the entire information on this field was distributed among 100 publications. Bearing in mind the fact that the role of patent literature has been continuously increasing (24% of the entire information in 1960 and 33% in 1970), the need for a working survey of this field of information becomes evident.

In the present review attention is concentrated on the publications of the 1970s (the earlier data have been largely covered in the monograph of Sheppard and Sharts [52] and also in Paleta's review [53], which include the literature for 1968 and 1969 respectively)—studies of fundamental importance or with an extensive bibliography.

The separate concluding section describes data on methods for the specific introduction of fluorine atoms into organic molecules, which is of specially great importance for investigators interested in applied chemistry.

One should note that the "Fluorine" information-research system, developed at the All-Union Institute of Scientific and Technical Information, significantly aided the authors in the selection of material for the review. A particularly valuable feature of this system is that it makes it possible to retrieve instantly detailed information about patent publications.

Certain references to the patent literature in the present review are based on data obtained from the above system.

II. THE FLUORINE ATOM AS A SUBSTITUENT

This section constitutes an attempt to survey the results of studies on organofluorine compounds by certain physical methods from the standpoint of their value for synthetic chemistry.

1. The Fluorine Atom at a Saturated Carbon Atom

The majority of applications of fluorocarbons and their derivatives enumerated in section I are associated with the extremely low polarity of these compounds and the consequent weakness of their intermolecular interactions. The quantities which determine the non-specific intermolecular interactions are molecular dipole moments and polarisabilities. The dipole moments of fully fluorinated alkanes with both normal and iso-structures are zero [54]. The introduction of only one hydrogen atom in the 1-position of the hexadecafluoroheptane molecule leads to the appearance of a significant dipole moment (1.60 D) and alkanes having the general formula $H(CF_2)_nH$, where $n = 4–10$, have dipole moments in the range 2–2.2 D. [55] On the other hand, 1,2-difluoroethane, a substance containing only two C–F bonds, is a liquid miscible with water. Its dielectric constant is 34.4 at 32 °C. [56] Evidently intermolecular H...F hydrogen bonds play a significant role in the solvation of 1,2-difluoroethane by water. The ability of fluorine atoms to form intramolecular hydrogen bonds is indicated by the infrared spectra of fluorine-containing alcohols and phenols [57] and also by the study of the structure of β-fluoroethanol by electron diffraction (90% of the *gauche*-conformation). [58]

The substitution of hydrogen atoms in alkane molecules by fluorine does not increase significantly their polarisability [59]. The weak solvation of fully fluorinated alkanes by various solvents is also consistent with these findings. It has been shown by ^{19}F NMR that dispersion interactions play a decisive role in this [60]: the dependence of the chemical shifts of CF_4, cyclo-C_4F_8, and cyclo-C_6F_{12} on the SV constant, characterising the properties of the solvent, is the same for both polar and non-polar media. The situation changes when chlorine or bromine molecules are introduced into the fluoroalkane molecule. The variation of the chemical shift in polar solvents becomes more pronounced owing to dipole–dipole interaction. It is significant that the chemical shifts of compounds usually employed as standards also change appreciably on passing from non-polar to polar solvents (the range of variation is 1.79 p.p.m. for CCl_3F, 1.88 p.p.m. for $C_6H_5CF_3$, and even as much as 4.88 p.p.m. for C_6F_6). [60] This fact is extremely important for investigators studying correlations in various solvents. The C_6F_6 chemical shift depends appreciably also on temperature: its change by 10 deg shifts the signal by 0.115 ± 0.021 p.p.m. [61]

Intermolecular interaction plays a significant role also in the chemical properties of organofluorine compounds. Thus the acidity of trihalogenoacetic acids in the gas phase varies in the sequence Br > Cl > F, i.e. in the order opposite to that widely known to hold for an aqueous medium. Evidently this finding is related to the greater polarisability of the bromine and chlorine atoms. On the other hand, in an aqueous medium the tendency of fluorine towards the formation of hydrogen bonds, leading to a more effective solvation of the trifluoroacetate ion, plays a decisive role [62].

Table 1. The binding energies of 1*s* electrons of the carbon atom in substituted methanes (in eV relative to CH_4). [63]

Formula	X = F	X = Cl	X = Br
CH_3X	2.8	1.6	1.0
CH_2X_2	—	3.1	—
CHX_3	8.3	4.3	—
CX_4	11.0	5.5	—

Photoelectronic spectroscopic data for halogenomethanes have shown that, as halogens accumulate, the binding energies of the electrons in the 1*s* level of carbon increase significantly, i.e. the formal atomic charge increases. This is particularly marked on accumulation of fluorine atoms [63] (the perfluoro-effect), which withdraw particularly strongly the valence electrons of carbon (Table 1). Photoelectronic spectroscopy can be used to analyse fluorine-containing polymers. The resolving power of existing instruments is sufficient to obtain resolved signals corresponding to the carbon atoms in the $CF_3–$, $–CF_2–$, $>CF$, and $–CH_2–$ groups. For this reason, it is possible to distinguish polymers with regular and irregular structures and by integrating the spectra one can also estimate the quantitative composition of the copolymers (for example $CF_2=CFCl$ can be distinguished from $CH_2=CF_2$). [64]

Quantum-mechanical calculations by non-empirical methods confirmed the increase of the charge of the carbon atoms in substituted methanes as fluorine atoms

accumulate (Table 2). Despite the appreciable difference between the charges obtained by different workers (the differences arise, in particular, from the choice of the *ab initio* set of wave functions, as shown by a methodological study[68]), the above tendency has been shown quite clearly in all investigations.

Table 2. The results of quantum-mechanical calculations on methane and its fluoro-derivatives.

Formula	Charge of C atom	Charge of H atom	Charge of F atom	References
CH_4	−0.114	+0.028		65
	−0.739	+0.185		65
	−1.104	+0.276	—	67*
	−0.751	+0.188		68*
	−0.076	+0.019		68*
CH_3F	+0.054	+0.029	−0.138	65
	−0.140	+0.174	−0.383	66
	−0.544	+0.296	−0.344	67*
	−0.129	+0.171	−0.385	68*
	+0.168	−0.004	−0.155	68*
CH_2F_2	+0.242	+0.022	−0.142	65
	+0.327	+0.175	−0.338	66
	+0.046	+0.317	−0.325	67*
CHF_3	+0.665	+0.184	−0.283	66
	+0.577	+0.344	−0.307	67*
CF_4	+0.936	—	−0.234	67*
	+0.68	—	−0.17	69

*Population data are quoted.

Fully fluorinated cycloalkanes behave as electron acceptors albeit to a slight extent. Thus the formation of charge-transfer complexes by these compounds with tetrakis(dimethylamino)ethylene has been demonstrated[70]. The reason for the enhanced (compared with linear analogues) electron-accepting properties of cyclic fluoroalkanes is probably that in their molecules the majority of the fluorine atoms are in the "eclipsed" conformation at short distances from one another. Under these conditions, the role of the interaction of the orbitals of these atoms, which may lower the thermodynamic stability of the molecule, becomes more marked. Nevertheless, owing to the pronounced screening of the positive charge of the carbon skeleton of the molecule by fluorine atoms, its chemical inertness can increase at the same time[71].

As will be shown below, the interaction between fluorine atoms plays an appreciable role also in the properties of fluoro-olefins.

The ability of fluoroalkanes containing bromine or iodine atoms to accept electrons is much more marked. The interaction of these compounds with mercury or amalgams[72], Grignard reagents[73], and the carbonyls of transition metals or their other derivatives in the lowest valence state[74] makes it possible to synthesise the corresponding σ-fluoroalkyl organometallic compounds. Nevertheless, the reaction between tertiary amines and fluoroalkyl iodides is not accompanied by irreversible electron transfer (leading ultimately to the formation of quaternary ammonium salts in the case of the usual halides—see Bubnov et al[75]) but consists merely in the formation of comparatively unstable complexes[76], which have been investigated by infrared[77] and NMR[78] spectroscopy.

Polarographic data have shown that fluoroalkylmercury derivatives are reduced at appreciably lower half-wave potentials than their hydrocarbon analogues (an electrochemical acidity scale has been constructed for hydrocarbons on the basis of these measurements[79,80]). The tendency of fluoroalkyl derivatives of mercury towards the formation of complexes with nucleophilic species is just as pronounced as their oxidising properties[81].

Thus the fluoroalkyl group, which exhibits a high electronegativity, reduces markedly the electron density at the metal atom to which it is linked. The resulting polarisation of the carbon–metal bond is evidently the main cause of the high, compared with non-fluorinated analogues, stability of fluoroalkyl σ derivatives of transition metals. Comparison of the photoelectronic spectra of $CF_3Mn(CO)_5$ and $CH_3Mn(CO)_5$[82] as well as the parameters of the NMR spectra of methyl and trifluoromethyl complexes of platinum[83] led to the conclusion that "back bonding", i.e. supply of the metal *d* electrons to the antibonding orbitals of the C–F bonds, does not play a significant role in the stabilisation of fluoroalkyl complexes.

The study of the relation between the parameters of ^{19}F NMR spectra of fluoroalkyl derivatives of mercury and the nature of the solvent revealed an anomalous behaviour of the *gem* constant for the $^{19}F-^{199}Hg$ spin-spin interaction, which decreases with increase of the solvating capacity of the medium (in contrast to the $^{19}F-^{199}Hg$ vicinal constant and the $^{1}H-^{199}He$ *gem* constant). This behaviour is evidence in support of the coordination of the mercury atom to the unshared electron pairs of the fluorine atom. This coordination, which lowers the capacity of mercury to combine with external nucleophiles, can play a significant role in the chemical behaviour of fluoroalkyl derivatives in metals[84].

The influence of the fluoroalkyl groups on the properties of the hydrocarbon groups bound to them is to a large extent determined by their strong negative inductive effect, which lowers the electron density at the adjacent carbon atoms. Conjugation effects play a certain role in aromatic systems. However, the absolute value of σ_I for fluoroalkyl groups exceeds significantly σ_R, which is of the same sign, the difference increasing with decrease of the number of fluorine atoms in the α-position, i.e. on passing from the CF_3 group to $C(CF_3)_3$, for which $\sigma_R = 0$ (see the review of Yagupol'skii et al.[85]). These data indicate the occurrence of a specific interaction between the π system and the orbitals of the fluorine atoms located in the benzyl position.

2. The Fluorine Atom at an Unsaturated Carbon Atom

The fluorine atom linked directly to an unsaturated carbon atom can both "strip" the multiple bond via the inductive effect and can supply to it electrons from its lone pairs. The acceptance of these electrons by the antibonding π* orbital should reduce the order of the C=C bond in fluoro-olefins, i.e. should lengthen it. However, owing to the inductive effect transmitted via the σ component, the length of the bond should diminish. As a result of the simultaneous action of these effects, the C=C bond in tetrafluoroethylene is nevertheless somewhat shorter than in ethylene[86]. According to photoelectronic spectroscopic data, the first ionisation potential (removal of a π electron) is virtually the same for ethylene and tetrafluoroethylene. Nevertheless the second potential (the removal of a σ electron from the C=C bond) of tetrafluoroethylene is higher by about 3 eV. On this basis, it has been concluded[87] that the filled orbitals of the fluorine atoms are mixed with the bonding π orbitals to an extremely slight extent and that the "perfluoro-effect" influences mainly the σ component of the C=C bond.

Furthermore, the overlapping of the p_X orbitals of the fluorine atoms, for example in the terminal CF_2 group, plays some role in the unusual properties of fluoro-olefins. This leads to the mutual approach of the fluorine atoms and the decrease of the angle between the C–F bonds to a value close to that of the tetrahedral angle[88] (previously this made it possible to attribute sp^3 hybridisation to the CF_2 group regardless of its environment[89]). The greater stability of *cis*-1,2-difluoroethylene compared with the *trans*-isomer has been explained similarly[88].

A chemical consequence of the dual effect of the fluorine atoms on the properties of the multiple bonds is electronic amphoteric properties of fluoro-olefins, i.e. their ability to react with both electrophilic and nucleophilic agents. As electronegative substituents accumulate at the multiple bond, the tendency to undergo nucleophilic reactions increases. A striking example of this is a reversal of the mechanism of the addition of nitrosyl fluoride on passing from tetrafluoroethylene (electrophilic process catalysed by BF_3) to hexafluoropropene (nucleophilic process catalysed by KF)[90]:

$$CF_2=CF_2+FNO \xrightarrow[BF_3,40^\circ]{} [\overset{\oplus}{C}F_2CF_2NO] \rightarrow CF_3CF_2NO\ , \qquad (9)$$

$$CF_3-CF=CF_2+FNO \xrightarrow[KF,80^\circ]{} \left[\begin{matrix}CF_3\\CF_3\end{matrix}\!\!>\!\overset{\ominus}{C}F\right] \rightarrow \begin{matrix}CF_3\\CF_3\end{matrix}\!\!>\!CFNO\ . \qquad (10)$$

In view of the reversal of the mechanism, it is possible to achieve the same reaction with the opposite mode of addition, depending on the nature of the catalyst. Thus, using the fact that perfluoromethyl vinyl ether is attacked by both electrophilic and nucleophilic agents at the CF_2 group, Lur'e et al.[91] succeeded in directing the mercury atom to the α- and β-positions in its molecule:

$$CF_3OCF=CF_2+HgCl_2 \xrightarrow[KF,20^\circ]{} [\overset{\ominus}{C}F_3OCFCF_3] \longrightarrow \underset{\displaystyle HgCl}{CF_3OCFCF_3}\ , \qquad (11)$$

$$CF_3\overset{\curvearrowright}{O}-CF=CF_2+HgF_2 \xrightarrow[HF,150^\circ]{} [CF_3O\overset{\oplus}{C}FCF_2HgF] \longrightarrow (CF_3OCF_2CF_2)_2Hg\ . \qquad (12)$$

Table 3. The full charges of the carbon atoms in fluoroethylenes.

Olefin	Group			References
	CH_2	CHF	CF_2	
$CH_2=CH_2$	−0.064			92
$CH_2=CHF$	−0.112	+0.218		92
	−0.046	+0.078		93
$CH_2=CF_2$	−0.138		+0.478	92
	−0.030		+0.219	93
$CHF=CF_2$		+0.121	+0.446	92
		+0.109	+0.235	93
$CF_2=CF_2$			+0.400	92

Quantum-mechanical calculations have shown that the charge at the olefinic carbon atom increases as fluorine atoms are attached to it, as happens in the series of saturated compounds (Table 3).

The results of the calculations of Borisova et al.[92] have not been confirmed by the familiar series of comparative reactivities of fluoro-olefins in reactions with nucleophilic and electrophilic agents:

ease of electrophilic reactions

$$\longleftarrow CH_2=CH_2 \quad CH_2=CHF \quad CH_2=CF_2 \quad CHF=CF_2 \quad CF_2=CF_2 \longrightarrow$$

ease of nucleophilic reactions

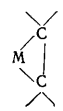
(on the other hand, according to these calculations vinylidene fluoride was the most reactive in any reaction).

Nevertheless the results obtained agree well with the measurements of the ^{13}C chemical shifts of fluoroethylenes, according to which the carbon atom of the CF_2 group of vinylidene fluoride is least shielded, while the carbon atom of the CH_2 group in the same compound is most strongly shielded[94] (Table 4).

Table 4. ^{13}C chemical shifts of fluoroethylenes (in p.p.m., quoted relative to ethylene).

Olefin	Group		
	CH_2	CHF	CF_2
$CH_2=CH_2$	0		
$CH_2=CHF$	+24.0	−24.94	
$CH_2=CF_2$	+58.22		−38.22
$CHF=CF_2$		+2.20	−25.24
$CF_2=CF_2$			−21.20

The calculated data quoted by Jolly and Perry[93] are remarkable in that the calculation of the binding energies of the 1*s* electrons of the carbon atom carried out on their basis makes it possible to estimate (in relation to experimental photoelectronic spectroscopic data) in which direction the calculated charge deviates. The distribution of the charges corresponds in this case to the series of comparative reactivities of fluoro-olefins in ionic reactions. The fairly stable π complexes formed by fluoro-olefins and transition metals are extremely promising from the standpoint of synthesis. The dative interaction, i.e. the supply of the *d* electrons of the metal to the antibonding π orbital of the olefin, makes the main contribution to the formation of the metal–olefin bond in this instance. However, the chemical behaviour of these complexes, frequently resembling that of small rings, and the relevant NMR data are described satisfactorily by formulae with two carbon–metal σ bonds (see Stone's review[95]):



The study of the properties of fluorine-containing dienes has shown that the conjugation of the multiple bonds in fully fluorinated 1,3-dienes is weakened. Thus comparison of the photoelectronic and ultraviolet spectra of 1,1,4,4-tetrafluorobutadiene and hexafluorobutadiene led to the conclusion[96] that there is a significant difference between their properties. Whereas the first compound has a *trans*-planar structure like normal butadiene, the second is not planar according to ultraviolet[96] and NMR[97] spectroscopic data. This conclusion has been confirmed by electron diffraction, which shows that the dihedral angle between the two $CF_3=CF$ groups in hexafluorobutadiene

is 47.4° ± 2.4°.[98] Evidently the breakdown of conjugation is associated with the interactions of the fluorine atoms in the CF groups.

The introduction of fluorine atoms into the aromatic ring also leads to the appearance of a significant positive charge at the carbon atom linked to it. Thus the ^{13}C NMR signal of hexafluorobenzene is displaced downfield by 38.34 p.p.m., compared with the signal of the 1-C atom of pentafluorobenzene[99]. Analysis of the photoelectronic spectra (the 1*s* levels of fluorine) has shown that the charge on this atom, linked to the ring, amounts to −0.15–0.20.[100] This is consistent with quantum-mechanical calculations (the charges in C_6F_6 are +0.132 for carbon and −0.132 for fluorine[93]). The changes in the charges of the carbon atoms which are not linked directly to fluorine are much smaller, amounting to zero for the *p*-position in fluorobenzene[100] and to −0.016 for the 9- and 10-positions in octafluoronaphthalene[101]. The ionisation potentials of the levels of aromatic fluoro-compounds (photoelectronic spectroscopy) differ from the corresponding values for the non-fluorinated analogues fairly slightly[102], i.e. the introduction of fluorine atoms does not prevent the aromatic system from retaining its capacity to behave as an electron donor. Indeed hexafluorobenzene forms charge-transfer complexes both with alkylbenzenes[103], behaving as an electron acceptor, and with the strong Lewis acid MoF_6,[104] behaving as an electron donor. Thus aromatic fluoro-compounds exhibit electronic amphoteric properties like fluoro-olefins.

The properties of the C_6F_5 group as a substituent are determined by the combination of the strong negative inductive effect (which is greater than for the C_6H_5 group but smaller than for CF_3) and the electron-donating properties associated with the presence of the lone electron pairs in the fluorine atoms. The electron-donating properties are manifested particularly clearly in the interaction of the C_6F_5 group with a cationoid reaction centre. The review of Vlasov and Yakobson[105] is devoted to a detailed consideration of these problems.

3. The Fluorine Atom in the Intermediate Species

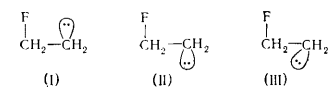
The mode and rate of a chemical reaction depend both on the structure of the reactant molecules and on the stability of the intermediate species formed. These two factors frequently act in different directions: the charge distribution in the attacked molecule can be unfavourable for the orientation leading to the formation of the more stable intermediate species. This effect is shown particularly clearly in reactions of organofluorine compounds: it has been shown that the charge separation between the atoms entering into the composition of their molecules is very pronounced.

For this reason, it is interesting to compare the stabilities of reaction intermediates with the observed mode of the processes, which has in fact been done below—mainly for fluoro-olefins. It is assumed that the findings obtained in the study of kinetically independent ions and radicals are valid also in these extremely common instances, where such species are not formed independently and there exists merely a transition state of the system which is of a type similar to them.

Among organofluorine compounds, reactions involving the intermediate formation of carbanions are most common. Despite their high electronegativity, fluorine atoms do not always stabilise these species, which is due to the presence of lone electron pairs in fluorine.

Thus, being bound directly to a negatively charged carbon atom, they can reduce significantly the stability of the carbanion as a result of the formation of the "back bond" between the electrons of the *p* orbital and the anionic centres. This phenomenon, sometimes referred to as the "Hine effect",[106] is evidently the cause of the decrease of the ionisation constant on passing from $CF_3CH_2NO_2$ to CF_3CHFNO_2[107] and also of the much lower kinetic acidity of $(CF_3)_2CHF$ compared with its analogues $(CF_3)_2CHX$ (X = Cl, Br, or I).[108]

The stabilisation of carbanions by the fluorine atoms in the β-position relative to the charged atom is difficult to account for exhaustively within the framework of the inductive effect. Calculation on the β-fluoroethyl anion, carried out in several versions using various semi-empirical approximations[109], has shown that the preferred conformations of the species are "*syn*" or "*anti*" (I, II), but not the "perpendicular" conformation (III), in which there is evidently a strong repulsion of the lone electron pairs of fluorine and the negatively charged carbon atom.



(I) (II) (III)

Analysis of the charge distribution among orbitals of the C–F bonds indicates a significant contribution of the π component, i.e. confirms the occurrence of "hyperconjugation" (an effect the nature of which requires further investigation). A non-empirical calculation on the FCH_2CH_2 cation, anion, and the radical led to analogous results. The preferred conformations are *syn*- or *anti*- for the anion and the perpendicular conformation for the cation[110]. As a result of the combination of these effects, tertiary monohydroperfluoroalkanes have an extremely "acid" hydrogen atom: according to deuterium exchange data, $pK_a = 11$ for $(CF_3)_3CH$,[108] and the value obtained in terms of the polarographic scale is as low as 7.[80]

It is believed[111] that the comparative reactivity series for the substituted benzenes $C_6F_5R_f$ in the reaction with ammonia [$R_f = (CF_3)_3C > CF_3CF_2 > (CF_3)_2CF > CF_3 \gg F$] indicates the absence of hyperconjugation in the intermediate species. However, since the σ_I for fluoroalkyl groups increase in the same direction[85], it may be that the higher reactivity of benzenes containing secondary and tertiary fluoroalkyl groups as substituents is associated merely with the greater positive charge in the *p*-positions in their molecules, which facilitates nucleophilic attack.

In contrast to carbanions, carbonium ions containing fluorine atoms at a charged carbon atom are stabilised. The lone electron pairs of the fluorine atoms are involved in "back bonding", as a result of which the fluoromethyl cations have a planar structure. The effect decreases somewhat (per fluorine atom) on passing from the CH_2F cation to CF_3. At the same time, the inductive effect of fluorine acting via the σ bond leads to an increase of the charge of the carbon atom from +0.659 in CH_2F^+ to +1.095 in CF_3^+ (calculation via the INDO method†)[112]. The ethyl cation with a fluorine atom in the β-position is less stable than the 1-fluoroethyl cation (the difference between the stabilisation energies is 29.23 kcal mole^{-1}). Its destabilisation compared with $C_2H_5^+$ can be partly compensated by the formation of the "non-classical" onium cation, $CH_2{-}CH_2$ with F which is more favourable on energy grounds than

† INDO = Incomplete neglect of differential overlapping.

the classical cation by 3.58 kcal mole^{-1}. However, in solution the more favourable species may be the more effectively solvated classical β-fluoroethyl cation (non-empirical calculations).[113]

Stabilisation as a result of the formation of a halogenonium cation is much more marked in the case of chlorine—the energy gain then amounts to 15.81 kcal mole^{-1}. This has been confirmed experimentally by the finding that the NMR spectrum of the β-chloroethyl cation at −80°C shows a singlet[114] (the applications of the NMR method in the study of fluorine-containing carbonium ions in highly acid media have been reviewed[115]).

The accumulation of fluorine atoms in the β-position relative to the positively charged carbon atom leads to the destabilisation of the cation compared with CF_3^+: whereas the ionisation potential of the $\dot{C}F_3$ radical does not exceed 9.5 V, it amounts to 9.98 V for $\dot{C}_2F_5$, 10.06 V for n-$\dot{C}_3F_7$, and 10.5 V for $(CF_3)_2\dot{C}F$ (mass spectroscopy).[116]

Quantum-mechanical calculations by the INDO method of the distribution of spin density in the series of radicals $\dot{C}H_3$, $\dot{C}H_2F$, $\dot{C}HF_2$, and $\dot{C}F_3$ showed that the unpaired electron density at the 2*s* orbitals of carbon and fluorine increases following the accumulation of fluorine atoms. This is consistent with the increase of the hyperfine interaction constants with the ^{13}C and ^{19}F nuclei in the ESR spectra of these radicals and also the change in their geometry, which gradually deviates from the planar structure of $\dot{C}H_3$.[117] On the other hand, owing to the high electronegativity of the fluorine atoms, the formal charge of the carbon atom in $\dot{C}F_3$ is +0.402 ($\sigma + \pi$, calculated from population data), while the charge in $\dot{C}H_3$ is 0.574.[118] Thus fluoroalkyl radicals should exhibit strong electrophilic properties. The enhanced stability of $\dot{C}F_3$ leads to a decrease of the energy of the C–C bond in hexafluoroethane to 60–70 kcal mole^{-1} compared with 79–81 established for alkanes. As a result, hexafluoroethane dissociates into radicals when acted upon by a glow discharge. Incidentally $(CF_3)_4Sn$ was synthesised by this unusual procedure (following addition to $C_2F_6SnI_4$), the yield exceeding 90%.[119] (Previously the C–C bond energy in C_2F_6 was assumed to be 94 kcal mole^{-1}; see Errede[120]. Possibly the C–H bond energy in CF_3H requires revision: the activation energy for the reaction of $\dot{C}F_3$ with alkanes, calculated on the basis of the value 106 kcal mole^{-1} adopted at the present time agrees poorly with the experimental results[121].)

In free-radical addition to fluoro-olefins an inconsistency is observed between the charge distribution in the initial molecule on the one hand, and the relative stabilities of the intermediate radicals on the other.

Thus, the addition of fluoroalkyl iodides to vinylidene fluoride or trifluoroethylene proceeds with a high degree of selectivity:

$$R_fI + CH_2{=}CF_2 \rightarrow R_fCH_2\dot{C}F_2I\ , \qquad (13)$$

$$R_fI + CHF{=}CF_2 \rightarrow R_fCHF\dot{C}F_2I\ . \qquad (14)$$

The selectivity increases on passing from $\dot{C}F_3$ to $\dot{C}_2F_5$ and $\dot{C}F(CF_3)_2$,[122] reaching in the latter case 97% for reaction (13) and 96% for reaction (14),[123] i.e. the process proceeds as if its mode were determined by the formation of the more stable radical $R_f\dot{C}H_2CF_2$. However, the opposite orientation is observed in the reaction of trifluoroethylene with the $\dot{C}H_3$ radical: the attack is directed to the CF_3 group to the extent of 88%.[124]

In the light of this finding, it becomes evident that the direction of attack on the olefin is not determined so much by the stability of the intermediate species as by polar effects. In the case of electrophilic fluoroalkyl radicals both factors act in concert, but the nucleophilic radical $\dot{C}H_3$ attacks trifluoroethylene via the carbon atom, which carries a more positive charge. In this connection the extremely high affinity of tetrafluoroethylene for $\dot{C}H_3$, which is ten times greater than in the case of ethylene[125] (the affinity of fluorobenzene exceeds that of benzene by a factor of 1.5)[126], is understandable.

Nevertheless in the reaction with an electrophilic species, such as the fluorine atom, the order of the reactivities of olefins is reversed: $CH_2{=}CHF > CH_2{=}CF_2 > CF_2{=}CF_2$ (kinetic data[127]).

The charge distribution in the ground state of the fluoro-olefin molecule is frequently of decisive importance also in ionic reactions. Thus in electrophilic addition reactions $\alpha\beta\beta$-trifluorostyrene gives rise to a mixture of products instead of the expected unambiguous result determined by the dominant stability of the benzyl cation[128]:

$$C_6H_5{-}CF{=}CF_2 + HBr \rightarrow C_6H_5CHF{-}CF_2Br + C_6H_5CFBr{-}CF_2H\ . \qquad (15)$$

Evidently the appreciable positive charge of the carbon atom in the CF_2 group, which hinders its protonation, has a significant influence in this case.

The stability of the recently synthesised enolic forms of the polyfluorinated ketones $CF_2{=}\underset{\displaystyle OH}{\underset{|}{C}}{-}CF_2X$, where X = F or Cl,[129] is apparently to some extent related to the difficulty of protonating the CF_2 group.

The stabilising effect which fluorine has on anion onoid species is also pronounced in the case of radical-anions:

$$R_2\dot{C}{-}OH \xrightarrow{-H^{\oplus}} [R_2C{=}O]^{\ominus}\ . \qquad (16)$$

Owing to the formation of the more stable ketyl, the acidity of the hexafluoro-2-hydroxyisopropyl radical (R = CF_3) exceeds that of hexafluoroisopropyl alcohol by 8.1 pK units, while the corresponding difference for R = CH_3 amounts to only 5.7 units[130].

The stabilising effect of fluorine leads to an increase of the hyperfine interaction constants for the ESR spectra of the radical-anions of fluorine-containing ketones[131] or nitro-compounds[132]. This constant is appreciably higher than for protons. Evidently the hyperconjugation effect plays a significant role in this[133]. ESR data for fluorocarbon radicals have been reviewed[134]. More recent data, obtained in liquid media, have been surveyed by Lloyd and Rogers[135].

The radical-cations derived from polyfluorinated benzenes are also stable. According to quantum-mechanical calculation (the INDO method), the charge on the carbon atom in $C_6F_6^{+\cdot}$ is +0.24 (cf + 0.132 in C_6F_6) and the unpaired electron density at the carbon atom is 0.12.[136]

The study of voltage–current curves in fluorosulphonic acid has shown that the radical-cations derived from pentafluorobenzene and 1,2,3,5-tetrafluorobenzene have lifetimes of the order of several minutes, while the radical-cations from hexafluorobenzene and octafluoronaphthalene exist in a highly acid medium for a very long time[137]. The formation of such radical-cations, which proceeds readily under the influence of antimony pentafluoride[138], apparently plays an important role in electrophilic reactions of aromatic fluoro-compounds (see, the review of Shteingarts and Yakobson[139]).

The influence of fluorine atoms on the properties of radicals is extremely important, because the radicals or the transition states resembling them are more common in the reactions of real organofluorine compounds than might have been supposed on the basis of traditional ideas

concerning the mechanisms of ionic processes. The transfer of single electrons, leading to the formation of radical species, frequently constitutes a decisive reaction stage. Biradical species (carbenes) and also triplet states of unsaturated systems, whose properties resemble those of biradicals, also play an extremely important role in reactions of organofluorine compounds.

Fluorine-containing carbenes are involved in many reactions of preparative value, particularly in pyrolytic industrial syntheses of fluoro-olefins. According to quantum-mechanical data (the Roothaan method), the positive charge on the carbon atom in carbenes, as in all other species, increases following the accumulation of fluorine atoms ($CF_2 > CHF > CH_2$). However, the presence of an unfilled π orbital in carbenes introduces its own specific features: its population also increases as a result of the interaction with the *p* electrons of the fluorine atoms. Since the interaction of the carbenes with unsaturated systems (the commonest type of reaction undergone by carbenes) probably begins with charge transfer to this orbital, the CH_2 group, in which the orbital is completely vacant, is more electrophilic than CHF. The electrophilicity of CF_2 is lower still and this carbene is one of the most selective[140].

On the other hand, the stability of the triplet states of aromatic fluoro-compounds is lower than for the analogues without fluorine. The study of laser flash photolysis of fluorobenzene has shown that the emission spectrum can be observed in the course of 250 ns (weaker approximately by a factor of two than the benzene spectrum), while the triplet state of pentafluorobenzene exists only in the course of 140 ± 5 ns.[141]

III. THE INTRODUCTION OF FLUORINE INTO ORGANIC MOLECULES

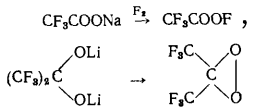
For a long time the introduction of fluorine atoms into organic molecules with the aid of an apparently natural reagent for this purpose such as free fluorine was regarded as virtually impossible in view of its extremely pronounced corrosive properties. Nevertheless, as early as 1933, the possibility of substituting by fluorine one hydrogen atom, for example in cyclohexane and carboxylic acids, or of the "fluorodimerisation" of tetrachloromethylene was demonstrated in a pioneer study by Bockemüller[142]:

$$2\,CCl_2{=}CCl_2 + F_2 \rightarrow FCCl_2CCl_2CCl_2CCl_2F\,, \qquad (17)$$

(subsequently this reaction was developed in detail for fluoro-olefins[143]); fluorination by free fluorine has not found extensive applications.

Only in recent years a number of reports have been published indicating the possibility of successful fluorination without degradation even of systems containing heteroatoms. Thus interesting peroxide compounds can be synthesised with the aid of fluorine[144,145]:

$$CF_3COONa \xrightarrow{F_2} CF_3COOF\,, \qquad (18)$$



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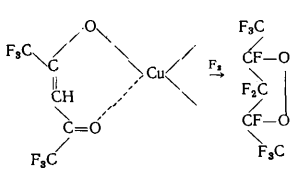


(20)

Fluorine atoms have been introduced successfully into the α-position with respect to the nitro-group by treating salts of nitro-compounds with fluorine (see Nagase's review[146]).

Direct fluorination shows promise of wide scale applications also in the synthesis of fully fluorinated fluoroalkanes and their derivatives used in practical applications. The reactor with a highly efficient heat elimination system, which has been developed for this process, makes possible exhaustive fluorination of complex compounds such as $(CH_3)_3C{-}C(CH_3)_3$,[147] $CH_3OCH_2CH_2OCH_3$,[148] or *m*-carborane[149]. The reaction is not accompanied by degradation and the yield of desired products is extremely high in the second and third instants.

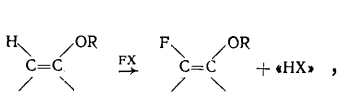
Fluorination by elemental fluorine is evidently a free-radical process. Its extremely high exothermic heat is associated with certain characteristics of the fluorine molecule, in particular with its low dissociation energy (37 kcal $mole^{-1}$ compared with 58 kcal $mole^{-1}$ for Cl_2).[150] In reactions with aromatic systems fluorine behaves as an electrophilic agent: despite the radical mechanism of the process, *ortho–para* orientation is observed predominantly for benzene containing substituents of the first kind[151-154] and *meta*-orientation for substituents of the second kind[151,152]. The selectivity of substitution characteristic of fluorine made it possible to achieve the preparative synthesis of the valuable antimetabolite 5-fluorouracil (see Section I) by direct fluorination of uracil[155].

Apart from direct fluorination, methods for the introduction of fluorine with the aid of a wide variety of fluorinating agents are widely used; in terms of their action on organic molecules, these can be divided into oxidative and non-oxidative.

1. Oxidative Methods for the Introduction of Fluorine

The development of methods for the specific introduction of fluorine atoms is clearly important for the synthesis of fluorine-containing physiologically active substances which have been finding increasing application in recent years. The possibility of modifying finished (for example natural) structures by treatment with a fairly mild fluorinating agent is particularly valuable. A number of agents, whose activity varies over a fairly wide range, have been developed for this purpose. Thus perchloryl fluoride ($FClO_3$) has been used successfully to fluorinate steroids[156] or penicillin derivatives[157] in the presence of bases. Comparison of $FClO_3$ with CF_3OF shows that the latter acts more vigorously[156]. Nevertheless fluorine atoms have been introduced successfully with its aid into griseofulvin[158] or an anhydro-sugar[159] (see Lustig and Shreeve[160] for a review of the chemistry of hypofluorites).

The mode of substitution when such agents are employed is usually determined by the presence of an electron-donating substituent at the multiple bond:



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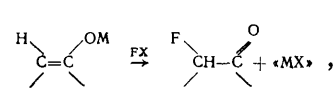
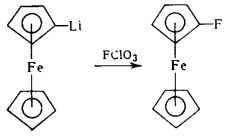


(22)

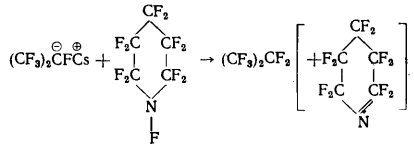
where M = Li or Na and X = OCF_3 or ClO_3.

The reaction with participation of hypofluorites frequently involves an addition–elimination stage[161]. However, direct fluorination of the anionoid centre is also possible[162]



(23)

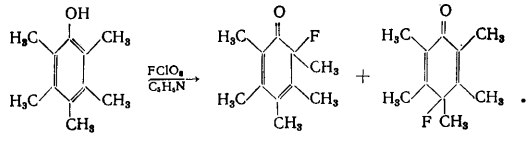
Perfluoropiperidine, a relatively weakly active agent, can act similarly (under severe conditions[163]):



(24)

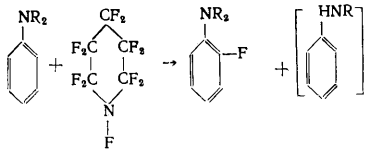
On the other hand, the activity of the bishypofluorite $CF_2(OF)_2$ apparently approaches that of free fluorine: it substitutes by fluorine the hydrogen atoms in acetonitrile or nitrobenzene[164].

Reagents of this type are used successfully also for the introduction of fluorine atoms into aromatic compounds. Thus CF_3OF substitutes one hydrogen atom in benzene or toluene. The reaction yield increases up to preparative values under the influence of intense ultraviolet irradiation. It is remarkable that the substitution in the toluene ring takes place almost exclusively in the *ortho*-position[165]. Xenon difluoride also reacts readily with benzene derivatives C_6H_5X with the preferential formation of *ortho*- and *para*-isomers for X = F, Cl, CH_3, or OCH_3 and *meta*-isomers for X = CF_3 or NO_2.[166] The formation of biphenyls is a side process. IF_4OCH_3 also shows a capacity for the fluorination of benzene rings[167]. In the fluorination by $FClO_3$ of phenols containing substituents in the *ortho*- or *para*-position, fluorodienones are formed[168]:



(25)

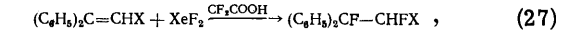
Perfluoropiperidine fluorinates *NN*-dialkylanilines exclusively in the *ortho*-position. Dealkylation and the formation of products of the type of Crystal Violet are side reactions[169]:



(26)

where R = CH_3 or C_2H_5.

In order to account for the orientation of the reactions enumerated above, a mechanism has been put forward involving substitution of the S_N2 type at the fluorine atom in the fluorinating agent[161,163]. However, the observation by ESR of the formation of radical-cations of aromatic compounds in the course of their fluorination by xenon difluoride[166] or perfluoropiperidine[169] and also the preferential or exclusive *ortho*-orientation of the substitution reaction established in a number of instances require a more detailed examination of this mechanism. Like many nucleophilic substitution reactions (see the review of Bilevich and Okhlobystin[170]), oxidative fluorination probably involves a stage in which a single electron is transferred. Nevertheless the radical-cations which can be detected are involved in the formation of side products only[171]. The fluorination of asymmetric diphenylethylenes by XeF_2 is not accompanied by a rearrangement (of the type usual in the generation of carbonium ions from these compounds) when the reaction is catalysed by CF_3COOH:

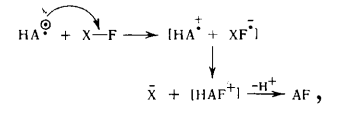


(27)

where X = H, F, or CH_3.

In catalysis by a stronger acid (HF) there is a partial rearrangement, which is probably not related to the fluorination process ($C_6H_5COCHXC_6H_5$ is formed)[172].

Thus fluorination can probably be regarded as a cage process, which involves the abstraction of a fluorine atom from the radical-anion formed by the molecule of the fluorinating agent. The process can be represented in the general form as follows (its outcome is indeed "substitution at the fluorine atom"):

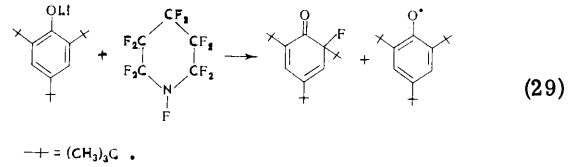


(28)

where HA is the fluorinated substrate with a lone electron pair and HF is the fluorinating agent.

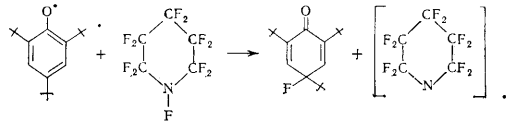
The following facts support this mechanism: if the potassium salt of nitroform is fluorinated by $FClO_3$ in the cavity of the ESR spectrometer in the presence of a radical "trap" (t-butylphenyl nitrone), radicals are formed as a result of the addition of both $(O_2N)_3C^{\cdot}$ and $F^{\cdot}$ to the nitrone. Consequently, the radical-anion $FClO_3$, capable of losing the fluorine atom, is formed after electron transfer[173].

Lithium 2,4,6-tris-t-butylphenoxide is rapidly fluorinated by perfluoropiperidine in the *ortho*-position:



(29)

A stable phenoxy-radical is formed as a side product; it cannot be an intermediate in the *ortho*-fluorination process, since it reacts very slowly with perfluoropiperidine (in the *para*-position):



(30)

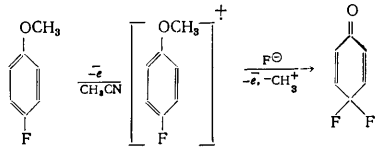
Thus *ortho*-fluorination is probably a process occurring within a cage and *para*-fluorination is a free-radical reaction[174]. The mechanism described is probably common for processes involving "anomalous" electrophilic substitution in aromatic compounds, leading to the preferential formation of *ortho*-isomers (see Pearson's review[175]).

The formation of radical-cations is probably a stage also in the fluorination by traditional agents such as the fluorides of metals in the highest valence state. Quantum-mechanical calculation has shown that the one-electron pathway in the fluorination of C_6F_6 under the influence of CoF_3 is more favourable on energy grounds than direct abstraction of a fluorine atom to an extent of the order of

50 kcal mole^{-1}.[136] Fluorination by lead tetra-acetate in HF is accompanied (as in the case of XeF_2 + HF) by a rearrangement of 1,1-diphenylethylene[176]:

$$(C_6H_5)_2C{=}CH_2 \xrightarrow[HF]{Pb(OCOCH_3)_4} C_6H_5CF_2CH_2C_6H_5 . \qquad (31)$$

The electrochemical generation of radical-cations of aromatic compounds in the presence of the fluoride ion also leads to the introduction of fluorine into the ring. Under these conditions, trifluoromethylbenzene is then substituted in the *meta*-position[177] and fluorobenzene is substituted in the *para*-position[178]. 4,4-Difluorocyclohexadienone is formed from *p*-fluoroanisole[179]:



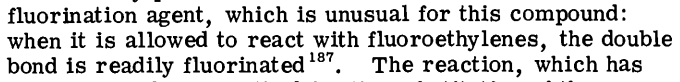
(32)

A similar mechanism may obtain also in the electrochemical fluorination of organic compounds in hydrogen fluoride[180], which is one of the most important industrial methods for the preparation of fully fluorinated organic compounds.

The widely used method for the introduction of fluorine into aromatic systems, involving the decomposition of solid diazonium salts containing the HF_4^-, PF_6^-, and SbF_6^- anions (Schiemann reaction, see Sushitskii's review[181]) probably also involves a one-electron transfer stage like the majority of typical reactions of diazo-compounds[182]. One of the most recent preparative versions of the Schiemann reaction, the photochemical decomposition of diazonium salts, frequently ensures a higher yield of aromatic fluoro-compounds than thermal decomposition[183].

The elimination of CO from benzoyl fluorides catalysed by rhodium complexes[184], the thermal elimination of SO_2F_2 from $C_6H_5OSOF_3$,[185] and also the elimination of groups such as SO_2 from $ArSO_2F$, CO_2 from ArOCOF, or COS from ArSCOF also leads to the introduction of fluorine into the aromatic ring. Examples of reactions of the latter type and also of the action of the fluoride ion on the diaryliodonium cation have been given in a patent[186] devoted to various methods for the synthesis of 4-(4′-fluorophenyl)-salicylic acid. This patent constitutes a kind of compilation of the modern methods for the introduction of fluorine into the benzene ring.

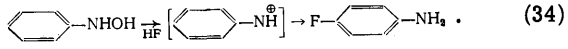
Antimony pentafluoride can behave as an oxidative fluorination agent, which is unusual for this compound: when it is allowed to react with fluoroethylenes, the double bond is readily fluorinated[187]. The reaction, which has been patented as a method for the substitution of the "residual" hydrogen by fluorine in hexafluoroepoxypropane oligomers, may also involve a stage in which the intermediate olefin is fluorinated[188]:



(33)

2. Non-Oxidative Methods for the Introduction of Fluorine

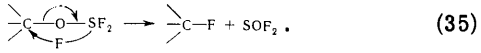
The introduction of fluorine may be a result of the formation of a cationoid species in a medium capable of supplying fluoride ions. Thus treatment of *N*-phenylhydroxylamine with HF leads to the formation of *p*-fluoroaniline[189]:



(34)

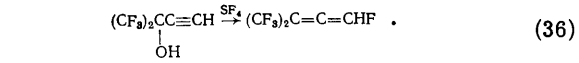
The reaction in which fluorine is introduced by means of sulphur tetrafluoride (a common reagent) and also its analogues (SeF_4,[190] $C_6F_5SF_3$,[191] R_2NSF_3,[192] and MoF_6[193]) also belongs to nucleophilic substitution processes.

These agents make it possible to convert smoothly the C–OH group into C–F, C=O into CF_2, and COOH into CF_3 or COF depending on the reaction conditions. It is suggested that the formation of the C–F bond is the result of an intramolecular nucleophilic substitution in the intermediate ester:



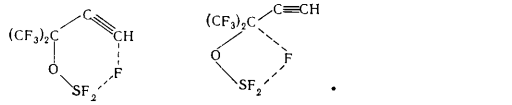
(35)

The side processes accompanying the fluorination by SF_4 are not inconsistent with this hypothesis. Thus, when unsaturated residues are present in the alcohol molecule, the following rearrangement is possible[194]:

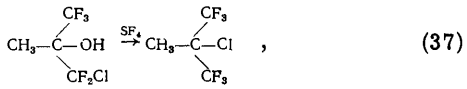


(36)

Evidently the driving force is the preferential formation on steric grounds of a six-membered transition state rather than a four-membered state leading to the normal product:

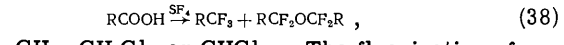


On treatment with SF_4, not only fluorination but also dehydration or rearrangement with transfer of the halogen can occur[195]:



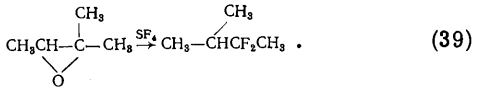
(37)

as well as the formation of ethers together with fluoroalkanes[196]:



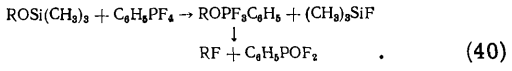
(38)

where R = CH_3, CH_2Cl, or $CHCl_2$. The fluorination of oxirans by SF_4 is also accompanied by rearrangements[197]:



(39)

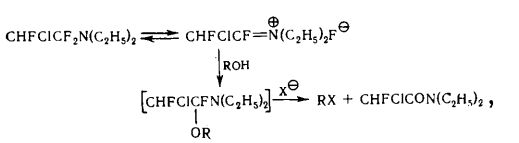
The new fluorinating agent $C_6H_5PF_4$, which smoothly replaces the $-OSi(CH_3)_3$ group by fluorine, probably acts similarly. The formation of intermediates in this case is facilitated owing to the high energy of the Si–F bond[198]:



(40)

The replacement of the hydroxy-group by fluorine with the aid of a mild agent such as the Yarovenko reagent $CHFClCF_2N(C_2H_5)_2$[199] (see Liska's review[200]) evidently also involves attack by the fluoride ion, which, however, is not intramolecular: in the presence of other nucleophilic species in the reaction medium, for example Cl^- or Br^-,

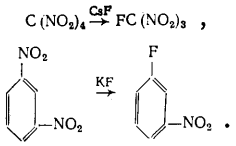
chlorine or bromine are introduced into the organic molecule instead of fluorine. The overall reaction mechanism involves the following stages[201]:



(41)

where X = F, Cl, or Br.

When the organic molecule contains a stable group which is eliminated, the latter can be replaced by fluorine also by means of the usual nucleophilic substitution. Fluorine has been introduced successfully in this way into carbohydrate molecules by the replacement of *p*-toluenesulphonyl[202] or methanesulphonyl[203] residues (see Podesva and Pacak[204] for a review of fluorocarbohydrates). The nitro-group can also be substituted[205,206]:



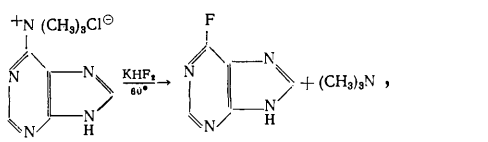
(42)

(43)

The substitution by fluorine of a nitro-group in purine and 1,2,4-triazole on heating with hydrogen fluoride[207] may involve the activation of the molecule by the protonation of the nitrogen atoms. A similar activation occurs in the *N*-methylation of 4-chloropyridine, which is then involved in halogen exchange with KF at 55°C.[208]

In the absence of activation, this reaction with polychlorinated aromatic (including heterocyclic) compounds requires very severe conditions (200–500°C). It constitutes the main method for the synthesis of polyfluorinated aromatic compounds (see Vorozhtsov's review[209]).

Heating of quaternary ammonium salts with alkali metal fluorides constitutes a promising method for the introduction of fluorine into heterocyclic compounds[210,211]:



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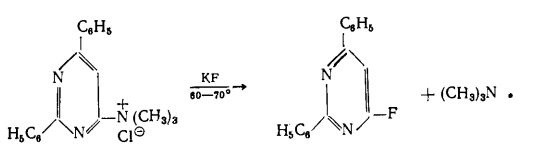
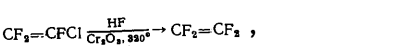


(45)

In many cases substitution of chlorine or bromine by fluorine requires the electrophilic cooperation of a "soft" Lewis acid, which binds the "soft" halogens. Such acids include SbF_3, SbF_5, HgF_2, AgF, and other agents used in this classical method for the introduction of fluorine, which is called the Swarts reaction (see the review of Fialkov and Yagupol'skii[212]). Chromium[213] and titanium[214] can also exhibit an electrophilic cooperation in the exchange of an olefinic halogen:



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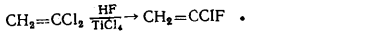
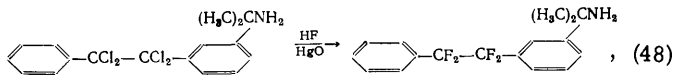


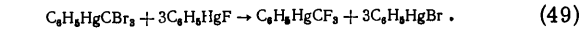
(47)

In the electrophilic cooperative action of mercury the halogen atoms in benzyl position are readily exchanged for fluorine[215]:



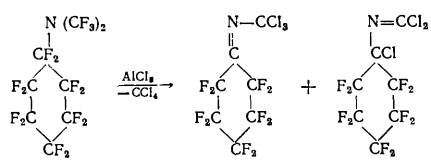
(48)

as well as those in the CBr_3 group linked to the mercury atom[216]:



(49)

However, since phenylmercury fluoride cannot undergo exchange with bromine in any other compound, reaction (49) may include a diahalogenocarbene transfer stage. "Hard" Lewis acids, i.e. derivatives of boron or aluminium, which form high-energy bonds with the "hard" fluorine atom, catalyse the reverse process—the exchange of fluorine for other halogens. Even certain fully fluorinated tertiary amines, which completely lack basic properties, enter into the reaction with $AlCl_3$, all the fluorine atoms in the α-position relative to the nitrogen atom being exchanged with elimination of CCl_4:[217]



(50)

Fluorine atoms in substituted trifluoromethylbenzenes are smoothly exchanged for chlorine with the aid of BCl_3 at 100°C,[218] while in the reaction with $AlCl_3$ the fluorine atoms in both vinyl and allyl positions in octafluorocyclobutene[219] and hexafluoropropene[220] derivatives are replaced.

During the preparation of this review for publication, a number of studies supplementing the data described here were published. The positive and negative ions derived from pentafluoroacetone and its stable enol have been investigated mass-spectrometrically[221]. In combination with ion cyclotron resonance, mass-spectrometry has been used to study the unusual decomposition of the pentafluoroallyl cation[222]. The stereochemical transformations of the corresponding radical have been studied by ESR[223]. New data on the inductive effect of fluorine atoms have been obtained with the aid of photoelectronic spectroscopy of a number of t-butyl alcohols[224]. Quantum-mechanical calculation[225] led to the conclusion that the fluorobenzenium ion is more stable when the fluorine atom is not attached to the sp^3-hybridised carbon atom. Experimental data indicating a greater stability of cycloalkyl carbonium ions containing a fluorine atom at the cationic centre in relation to analogues containing a chlorine atom have been obtained[226]. The one-electron mechanism of the interactions between arylethylenes and lead dioxide in SF_4 or HF has been confirmed by ESR[227].

Examination of new data for the reactions of organofluorine compounds will be the subject of a separate review.

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* Here and henceforth the asterisk denotes patents quoted after the "Fluorine" Information-research System.

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The Siloxane Bond and Its Influence on the Structure and Physical Properties of Organosilicon Compounds

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The main characteristics of the structure of the siloxane bond are examined and the results of studies on the structures and properties of oxygen-containing silicon compounds by physical methods are reviewed.
The bibliography includes 405 references.

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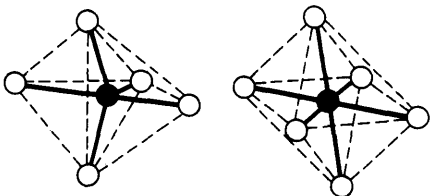
I. INTRODUCTION

Polymeric organic and inorganic silicon compounds have found recently a wide variety of numerous practical applications. The valuable properties of these compounds, the microstructure of which is based on alternating silicon and oxygen atoms, are due primarily to the nature of the siloxane bond $\geq$Si—O† in all silicon(IV) compounds. This bond is formed as a result of σ coupling of the hybridised s and p electrons of the silicon atom with the p electrons of oxygen; there is then the additional possibility of π interaction between the unshared p electrons of the oxygen atom and the $3d$ orbitals of silicon, which has been called p_π—d_π or $(p \rightarrow d)_\pi$ coupling.

The formation by s and p electrons of four tetrahedral σ bonds involving the silicon atom makes the latter similar to its immediate neighbour in the Periodic System—carbon. However, the possibility of $(p \rightarrow d)_\pi$ bonding introduces sharp differences between the structures and properties of the corresponding silicon and carbon compounds, Silicon, an element of the Third Period, has free $3d$ orbitals corresponding to the M shell and is therefore capable of functioning as an electron acceptor in the formation of a donor—acceptor d_π—p_π bond. However, research on organosilicon compounds in the course of more than 100 years has shown that at normal temperatures silicon does not form multiple p_π—p_π bonds.

Since, in contract to the p orbitals, not all the $3d$ orbitals have the same form and relative orientation in space, more than two d orbitals of the silicon atom cannot be used in its combination with the atoms of other elements, probably because of geometrical factors[2-4]. As a result, the maximum coordination number of silicon is six[4]. In hexacoordinate complexes the silicon atom has $3sp^3d^2$-hybridised orbitals and in pentacoordinate complexes it has $3sp^3d$-hybridised orbitals.

The angular functions of the d orbitals enable silicon to form a wide variety of σ and π bonds with other elements. However, according to quantum-chemical calculations the d orbitals in the free atoms of elements in the Third Period are too diffuse for the formation of σ bonds. Such bonds can be formed only when there are electronegative substituents at the silicon atom in the molecule, which can increase its effective positive charge. The $3d$ orbital is then compressed and becomes of comparable size to the $3s$ and $3p$ orbitals[2-4]. Of the five d orbitals only the d_γ orbitals ($3d_{z^2}$ and $3d_{x^2+y^2}$) can be used for the formation of σ bonds. Their hybridisation with the $3s$ and $3p$ orbitals can lead to several structures. The bipyramidal form (I), characteristic of the complexes of pentacovalent silicon, is stabilised by the hybridisation of the s and p orbitals with the d_{z^2} orbital[5]. The octahedral structure (II) is characteristic of the coordination compounds of hexacovalent silicon[5,6].



(I) (II)

The d_ϵ orbitals ($3d_{xz}$, $3d_{yz}$, and $3d_{xy}$) are involved in d_π—p_π bonding. In contrast to the p_π—p_π bond, this type of multiple bond does not prevent free rotation about the σ bond. A consequence of this is the relatively high freedom of rotation about the siloxane bond.

Numerous pieces of physical evidence for the occurrence of the $(p \rightarrow d)_\pi$ interaction between the silicon and oxygen atoms joined by the siloxane bond are considered below. The wide variety of the reactions involving the cleavage of the Si—O bond, related in one way or another to its $(p \rightarrow d)_\pi$ character, are of independent interest and are not considered in this review.

† The term "siloxane bond" was introduced into the nomenclature of organosilicon compounds by Stock[1] in 1917 to designate the linkage between the silicon and oxygen atoms. It is present in all silicon compounds of the type $\geq$Si—O—R, where R = —Si$\geq$H, a hydrocarbon group acyl group, metal, etc.

II. STRUCTURAL AND PHYSICAL CHARACTERISTICS OF THE SILOXANE BOND

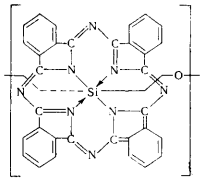
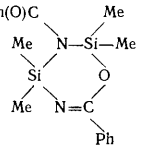
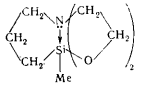
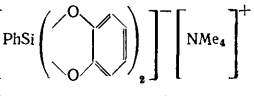
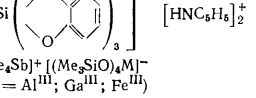
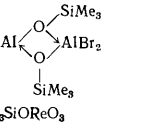
1. Interatomic Distances and Valence Angles

The Si—O bond lengths and SiOR valence angles in organic siloxanes are listed in Table 1. According to the tabulated data, the Si—O bond length is 1.64 ± 0.03 Å in the vast majority of organic silicon derivatives. This value is much lower than the Si—O bond length calculated assuming the additivity of the atomic radii (1.83 Å; the atomic radii of silicon and oxygen are 1.17 and 0.66 Å respectively)[56].

Table 1.

No.	Formula	Si-O bond length, Å	SiOR angle, deg	Method of determination	References
1	2	3	4	5	6
1	$(H_3Si)_2O$	1.633±0.001	144±1	—	7
		1.634±0.002	144.1±0.8	e	8
		—	~180	sp	9
		—	135—155	sp	10
		—	<180	sp	11
2	$(D_3Si)_2O$	—	~180	sp	9
3	$(Me_3Si)_2O$	—	140	sp	12
		—	137±7	sp	13
		1.65—1.66	130	x	14
		1.63±0.03	130±10	e	15
		1.63±0.05	130±10	e	16
		—	148	sp	17
4	$(Cl_3Si)_2O$	1.64±0.03	—	e	15, 16
		—	160—170	sp	18
5	$(F_3Si)_2O$	1.58±0.03	155.7	e	19
6	$Si(OSiMe_3)_4$	1.63	140±5	e	16, 20
7	$R(R_2SiO)_4SiR_3$ (R = Me, Et)	1.65—1.66	130	x	14
8	$H(Me_2SiO)_nOH$ ($n \geqslant 1000$)	1.64	130	x	21
9	Rubber based on polydimethylsiloxane raw rubber	—	140±10	x	22
10	$(Me_2SiO)_3$	1.66±0.04	125±5	e	23, 24
11	$O(Me_2SiO)_2Si(OSiMe_2)_2O$	1.64±0.03	130±5	x	25
12	$(Et_2SiO)_3$	1.65	125	x	14
13	$Me_2SiCH_2Si(RR')CH_2SiMe_2$ (R', R' = Me, Et, Ph)	—	125	sp	26
14	$Me_2Si(CH_2)_2Si(Me)R$ (R = Me, Pr, Bu, Ph)	—	120	sp	26
15	$Me_2SiCH_2—N(CH_2CH_2X)(CH_2SiMe_2)$ (X = NH_2, $NHCH_2CH_2NH_2$, OH)	—	110—115	sp	27
16		—	105	sp	26
17	$Me(Ph)SiCHCHSi(Ph)Me$ (R = H, Ph)	—	105	sp	26
18	$(Me_2SiO)_4$	1.66	140	x	14
		1.65	142.5	e	20
		1.63	140±5	e	28
19	$(Et_2SiO)_4$	1.66	140	x	14
20	$(Me_2SiO)_5$	1.66	145	x	14
21	$(Me_2SiO)_8$	—	—	x	29
22	$Me_8Si_8O_8$	1.63±0.04	136±2	x	30
23	$(Me_8Si_4O_8)_2$	1.65	148, 133	x	31
24	$(Me_4Si_2O)_2$	1.61	143.2	x	32
25	$(MeSiO_{1,5})_8$	1.61	145	x	33

Table 1 (contd.)

No.	Formula	Si-O bond length, Å	SiOR angle, deg	Method of determination	References
1	2	3	4	5	6
26		1.66	—	x	34
		—	150	x	35
		—	180	x	36
27	$Si(OMe)_4$	1.65	—	e	37
		1.64±0.03	113±2	e	15, 16
28	$MeOSiH_3$	1.64±0.003	120.6±0.9	e	38
29	$PhOSiH_3$	1.648±0.007	121±1	e	39
30	$Me_2Si(OH)_2$	1.63	—	x	40
31	$Et_2Si(OH)_2$	1.63±0.02	—	x	41—43
32	Me_3SiOM (M = K, Rb, Cs)	1.60—1.61	123±2	x	44
33		1.670	—	x	45
34		1.663 1.669	—	x	46
35	$PhSi(OC_6H_4)_3N$	1.635 1.650	— —	x	47
36	$m\text{-}O_2NC_6H_4Si(OCH_2CH_2)_3N$	1.656, 1.661 and 1.650	122—123	x	48
37	$PhSi(OCH_2CH_2)_3N$	1.638, 1.664 and 1.665	—	x	8, 49
38		1.700 and 1.794	—	x	50
39		1.813, 1.765 and 1.775	—	x	51
40	$[Me_4Sb]^+[(Me_2SiO)_4M]^-$ (M = Al^{III}; Ga^{III}; Fe^{III})	1.56	147	x, PMR	52, 53
41		1.70	130	x	41, 54
42	$Me_3SiOReO_3$	1.69	164±5	x	55

*e = electron diffraction, sp = spectroscopic, x = X-ray diffraction.

In the dimeric molecule of dibromotrimethylsiloxyaluminium (compound 41 in Table 1), in trimethylsilylperrhenate (compound 42), and in tetra-alkylammonium (compound 38) and pyridinium (compound 39) siliconates the Si—O bond is longer than in the majority of organosilicon derivatives (1.7—1.8 Å), while in hexafluorodisiloxane (compound 5) and in tetramethylstiboniumtetrakis(trimethylsiloxy)-derivatives of metals (compounds 40) it is shorter (1.56 Å). In inorganic silicon derivatives (silicates) the Si—O distances vary over the range 1.54—1.78 Å.[7,57-61]. The Si—O bond is shortened in all silicon

compounds containing the Si—O—M group, where M is a metal atom with an effective positive charge (silicates, siliconates, and siloxanolates)[62]. In alkali metal trimethylsilanolates (compounds 32) the Si—O bond length is about 1.60 Å.

On the other hand, in the disiloxane linkage in silicate anions, the silicon atoms of which are joined in an anionic oxygen atom (Si—O⁻), the interatomic Si—O distance is longer than usual (1.75—1.85 Å).[59-62] The Si—O bond is lengthened (1.7—1.8 Å) also in organic silicon compounds where the oxygen atom is linked to an electron-accepting substituent (compounds 38—42 in Table 1).

The decrease of the Si—O bond length noted above cannot be accounted for solely by its appreciable ionic character, since the introduction of the appropriate correction for the difference between the electronegativities of the silicon and oxygen atoms leads to 1.77 Å.[62] The shorter length of the Si—O bond convincingly demonstrates its partial double bond character arising as the result of the $(p \rightarrow d)_\pi$ interaction. The degree of double bond character (bond order) depends on the nature of the substituents at the silicon and oxygen atoms. Electron-accepting substituents at the silicon atom, which decrease the energy of the 3*d* orbitals, or metal and oxygen atoms, which increase the effective negative charge of the silicon atom, increase the Si—O bond order. On the other hand, electron-donating substituents at the silicon atom or electron-accepting groups at the oxygen atom decrease the siloxane bond order.

Although no compound is known in which the silicon atom is joined to an oxygen atom by a double bond, presumably the order of the "short" Si—O bonds (1.56 ± 0.03 Å) approaches that of the double bonds Si=O as a result of the additional $(p \rightarrow d)_\pi$ interaction. In long Si—O bonds (1.7—1.8 Å) the degree of $(p \rightarrow d)_\pi$ coupling is reduced to a minimum and they can be regarded as virtually single bonds. On the other hand, in the majority of organosilicon compounds the Si—O bond (1.64 ± 0.03 Å) is 40—50% ionic[62,63] and its order is 1.2—1.5.[62]

The valence angle between the oxygen bonds increases in the sequence H_3COCH_3 (111.43°)[64] < H_3SiOCH_3 (120.6°)[38] < $H_3SiOSiH_3$ (144.0°).[8] This demonstrates an increase of the amount of *s* character of the oxygen σ orbitals. When oxygen combines with one and two silicon atoms (in methoxysilane and disoloxane), its hybridisation is the average between sp^3 and sp^2 and between sp^2 and *sp* respectively. The increase of the SiOSi angle, associated with the transition from the sp^3 hybridisation of the oxygen atom to sp^2 and to *sp*, in the limiting case, probably favours the formation of common mutually perpendicular π orbitals between the two lone pairs of the oxygen atom and the *d* orbitals of the two silicon atoms linked to them (Fig. 1).

The SiOC angles in methoxy- and phenoxy-silanes (compounds 28 and 29) are almost identical. In tetramethoxysilane (compound 27) the SiOC angle (113°) is smaller than in methoxysilane, which indicates a marked weakening of the interaction between the *p* electrons of each of the four oxygen atoms and the *d* orbitals of silicon as a result of the competing mutual influence of the methoxy-groups.

The SiOSi angle varies within very wide limits; from 105° (compounds 16 and 17) to 150—170° in hexahalogenosiloxanes (compounds 4 and 5) and from 125° to 180° in silicates[58,59,61]. The great flexibility of the SiOSi angle, which in the vast majority of silicon compounds is much greater than the tetrahedral valence angle of oxygen in the state of sp^3 hybridisation (109°), is not inconsistent with the presence of the $(p \rightarrow d)_\pi$ bond between oxygen and silicon, since the five orthogonal diffuse 3*d* orbitals of the latter make it possible to form π bonds for any steric orientation of oxygen.

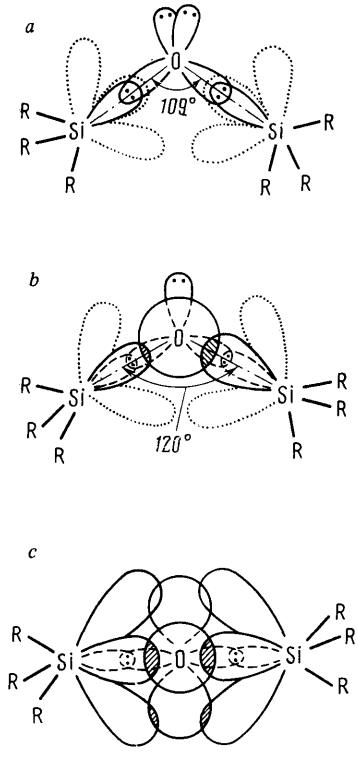
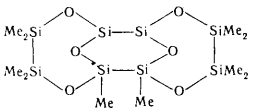


Figure 1. The overlapping of the electron orbitals of an sp^3-, sp^2-, and *sp*-hybridised oxygen atom (*a*, *b*, and *c* respectively) with the orbitals of the silicon atoms in the disiloxane group.

With increase of the SiOSi angle, the SiO bond length diminishes and its order increases. A decrease of the SiO (Si) bond length by 0.02—0.03 Å corresponds to an increase of the SiOSi angle in silicates by 10°.[61]

The SiOSi angles in the planar six-membered rings of the silicate anions $[Si_3O_9]$ (Lazarev[61]) in cyclotrisiloxanes (compounds 10 and 12) and in octamethylspiropentasiloxane (compound 11) are 125—130°. In contrast to the planar cyclotrisiloxanes[14,23-25], cyclosiloxanes containing more than three siloxane units are non-planar[14,20,28,29]. In cyclosiloxanes consisting of more than three siloxane units (compounds 18—22), in silsesquioxanes (compound 25), and also in linear (compounds 8 and 9) and branched (compound 6) siloxanes the SiOSi angle is somewhat greater (130—145°). In the phthalocyaninesiloxane polymer (compound 26) the SiOSi angle is probably close to 180° owing to the steric hindrance due to the phthalocyanine groups[35,36]. In disiloxanes (compounds 1—5) the SiOSi angle varies in the range 135—156° according to electron diffraction data. We may note that indirect spectroscopic methods lead to unduly high values of these angles (155—180°, Table 1). The maximum SiOSi angle

(155.7°) has been observed, as expected, in hexafluorodisiloxane (compound 5), which contains the most electronegative substituents (fluorine atoms) at the silicon atoms.

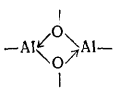


Two types of SiOSi angles were found in compound 23; 133° in the planar six-membered ring and 148° in the nonplanar seven-membered rings.

In contrast to the SiOSi angle, the OSiO angle in the majority of organosilicon compounds varies within narrow limits (110—120°).[14,20,21,23-25,28-33,40-43] In silanediols it amounts to 110° ± 2°.[40-43] In the five-membered ring of compounds 38 and 39, which have an ionic structure, the OSiO angle is 86—90°.[50,51] One oxygen atom of each five-membered ring occupies an equatorial position and the other is in an axial position, the axial SiO bonds (1.794 Å), being significantly longer than the equatorial bonds (1.700 Å).[50]

According to X-ray diffraction data, the geometrical shape of silatrane molecules (compounds 34—37), containing a pentacoordinate silicon atom, is that of a distorted trigonal bipyramid (with respect to the silicon atom) with equatorial oxygen atoms[49]. The SiOC angles in *m*-nitrophenyl-(2,2′,2″-nitrilotriethoxy)silane (compound 36) are 122—123°. The atrane half-rings in silatranes are completely identical, have a non-planar configuration, and are extremely mobile[49].

The SiOM angles (M = metal) in silicates and in organosilicon compounds are always greater than 120°. In the dimeric dibromotrimethylsiloxyaluminium molecule (compounds 41) the four-membered ring



is planar and the SiOAl angle is 130°. Tetramethylstibonium tetrakis(trimethylsiloxy)aluminate (compound 40), which forms orthorhombic crystals with two molecules per unit cell, has an ionic structure: the SiOAl angle is 147°.[52,53] In trimethylsilyl perrhenate (compound 42) the SiORe angle is 164°.[55]

As in t-butoxides, in tetrameric potassium, rubidium, and caesium trimethylsilanolates (compounds 32) the SiOM angle is 123° ± 2°.[44] According to cryoscopic and ebullioscopic data, alkali metal (Li, Na, or K) siloxanediolates are dimerised[65].

2. The Bond Energy

The siloxane bond is one of the most stable bonds formed by silicon and is inferior in this respect only to the Si—F bond. The Si—O bond strength calculated from heats of combustion has been estimated, the results ranging from 101 to 118 kcal mole^{-1} (Table 2). It is much lower than the value (242.4 kcal mole^{-1}) predicted by theory for the $Si^+ - O^-$ ionic bond[66]. The much higher energy of formation of the Si—O bond compared with the less polar C—O bond and the more polar Ge—O, Sn—O, and Pb—O bonds evidently indicates the occurrence of $(p \rightarrow d)\pi$ interaction between silicon and oxygen‡.

According to the data in Table 2, the Si—O (Si) bond energy is probably somewhat greater than the Si—O (C) bond energy.

Table 2. The siloxane bond energies.

No.	Formula	Si-O bond energy*, kcal mole^{-1}	References
1	$(Me_3Si)_2O$	117 112	12 68
2	$Me_3SiOSi(Me)_2OSiMe_3$	117 115	12 68
3	$Me_3Si[OSi(Me)_2]_2OSiMe_3$	117	12
4	$Me_3Si[OSi(Me)_2]_3OSiMe_3$	117 118	12 68
5	SiO_2	112	69
6	$(Me_2SiO)_4$	108	68
7	$(MeO)_4Si$	102	70, 71
8	$[(MeO)_3Si]_2O$	101	70, 71
9	$[(MeO)_2SiO]_2Si(OMe)_2$	102	70, 71
10	$[(MeO)_3Si]_2$	101	70, 71

* See Refs. 12 and 70—79 for the heats of combustion and formation of compounds containing the Si—O bond.

The heats of formation ΔH, entropies S, and heat capacities C_p of compounds containing the siloxane bond have been calculated very accurately according to an additive scheme[78]. For organosilicon compounds in the ideal gas state at 25° and 1 atm, ΔH_{Si-O} = −52 kcal, C_p = 9.6 cal g^{-1} deg^{-1}, and S = −1.24 eu.[78]

It has been shown for cyclodimethylsiloxanes and cyclomethyl(isopropoxy)siloxanes[79] that the Si—O bond energy in cyclosiloxanes depends on the number of siloxane units in the ring. The Si—O bond energies in cyclotetrasiloxanes and cyclopentasiloxanes, which have relatively unstrained rings, and in linear siloxanes are close to one another. The appreciable strain of the rings in cyclotrisiloxanes leads to an increase of the Si—O bond energy (to 9 kcal mole^{-1}).[79]§ The difference between the Si—O bond energies in cyclotrisiloxanes and cyclosiloxanes with large rings has been confirmed by the heats of their catalytic cleavage reactions. The heat of opening the D_3 ring is 3—4 kcal mole^{-1}.[81-83] Calorimetric measurements revealed a slight (to the extent of about 0.2 kcal mole^{-1}) strain of the rings in D_4 and D_5.[82] When the methyl groups in cyclodimethylsiloxanes are replaced by propyl or 3,3,3-trifluoropropyl groups, the heat of ring cleavage increases. The ring strain energy reaches 5.25 kcal

‡ The bond strength (and force constant) usually increase with increase of bond polarity. In the case of C—O the $(p \rightarrow d)\pi$ linkage cannot be formed (there is no 2*d* orbital). The Sn—O bond has a markedly ionic character and is more than 50% longer (2.30 Å) than the Si—O bond. Therefore the formation of $(p \rightarrow d)\pi$ linkages with participation of the 5*d* electrons of tin is greatly hindered[67].

§ The conclusion reached on the basis of measurements of diamagnetic susceptibility that the ring strain in D_3 and D_4 [80] is identical must be regarded as erroneous. (D = Me_2SiO).

mole^{-1} in F_3¶ and 1.3 and 0.75 kcal mole^{-1} in F_4 and F_5 respectively.[82]

In the compounds $R^1R^2\overset{\overset{\Large O}{\frown}}{Si}CH_2CH_2SiR^3R^4$, where R^1, R^2, R^3, and R^4 = Me or Ph, the ring strain increases on replacement of methyl groups by phenyl groups. The heat of polymerisation of these compounds, which involves the dissociation of the Si—O bond, is 8—12 kcal mole^{-1}.[81]

Since the equilibrium ratio of the cyclosiloxane stereoisomers is in all cases without exception close to the statistical value[84-91], presumably the Si—O bond energy is the same in all the isomers of this cyclosiloxane. This hypothesis agrees well with the conclusion that the rates of polymerisation of F_3,[92] P_3, P_2D,[93] A_2D, A_3, A_2D_2, A_3D, and A_4 [94,95] stereoisomers are similar†. Therefore the enthalpies of the A_3(ΔH_{cis} = 27 kcal mole^{-1} and ΔH_{trans} = 22 kcal mole^{-1}) and A_4 (ΔH_{cis} = 8 kcal mole^{-1} and for the remaining three isomers ΔH = 0) stereoisomers, obtained from the temperature variation of the equilibrium constants for their interconversion[90], appear to be unexpected. The difference between the enthalpies of the A_3 and A_4 stereoisomers is not consistent with their statistical distribution at equilibrium, established in the same study[90].

3. Dipole Moments

The dipole moments μ of linear[96-110] and cyclic[97,100,111-114] siloxanes, silanols[103,115-117], alkoxysilanes, acyloxysilanes[118-131], and silatranes[132-135] have been largely compiled in the handbook of Osipov et al.[136] The experimental dipole moments of the linear siloxanes $Me_3SiO(D)_nMe_3$ and cyclosiloxanes D_n with a large number n of siloxane units in the ring agree well with the values calculated by the empirical formula[97] $\mu = 0.7\sqrt{n}$.

The dipole moment of D_3, which has a planar strained ring, is zero[100]. The configuration of the F_3 stereoisomer has been established on the basis of the dipole moments (expressed in D). The compound with μ = 4.7 D is the *cis*-isomer and that with μ = 2.98 D is the *trans*-isomer[87].

The dipole moments of disiloxanes are comparatively small (0.24—1.03).[96-105] The SiOSi angle calculated from the dipole moments of disiloxanes is much greater than the tetrahedral value: 160 ± 15° [97] (131° [102]) in hexamethyldisiloxane and about 180° [96] in disiloxane (this value is evidently too high).

As already stated, an increase of the SiOSi angle indicates an increase of the Si—O bond order. The dipole moment of the Si—O bond, calculated from the dipole moments of disiloxanes[96,97,100] and branched[13], linear[137], and cyclic siloxanes[100] and alkoxysilanes[118], is 1.2—1.65 D. Judging from the dipole moment, the polarity† of the Si—O bond is much lower than might have been expected bearing in mind the large difference between the electronegativities of silicon (1.89) [63] and oxygen (3.50).[63]

The group dipole moment increases in the series $\mu_{H_3SiO} < \mu_{Me_3SiO} < \mu_{Ph_3SiO}$. The value of μ_{H_3SiO} in disiloxane is 0.28—0.40 D [96] and μ_{Me_3SiO} amounts to 0.95—1.05 D in alkoxytrimethylsilanes[13,101,102] and 1.3 D in hexamethyldisiloxane[101]; μ_{Ph_3SiO} in hexaphenyldisiloxane is 1.2—1.7 D.[104] The smaller group dipole moment of Me_3SiO in alkoxytrimethylsilanes compared with hexamethyldisiloxane is due to the different polarities of the Si—O bond and the different types of $(p \rightarrow d)_\pi$ interactions between the oxygen and silicon atoms.

The dipole moments of methoxymethylsilanes in the series $Me_{4-n}Si(OMe)_n$ are greater than for hexamethyldisiloxane and increase with increase of n:[13]

$$\mu_{(Me_3Si)_2O} < \mu_{Me_3SiOMe} < \mu_{Me_2Si(OMe)_2} < \mu_{MeSi(OMe)_3} < \mu_{Si(OMe)_4}.$$

The dipole moments of tetra-alkoxysilanes $Si(OR)_4$ with branched alkyl groups are smaller than those of tetra-alkoxysilanes with normal alkyl groups and with increase of the degree of branching μ falls. The dipole moments of mixed alkoxysilanes having the general formula $(MeO)_nSi(t\text{-}Bu)_{4-n}$ vary linearly with n.[127]

The dipole moments of methoxymethylsilanes[13,118] and tetra-n-alkoxysilanes[118,129] agree satisfactorily with the values calculated for the tetrahedral model of these compounds, which postulates free rotation about the Si—O bond. In the presence of two or more phenoxy-groups at the silicon atom[128] or of branched alkoxy-groups in trialkoxyphenylsilanes[124], the rotation about the Si—O bond is greatly restricted. Free rotation about the siloxane bond in tetra-n-alkoxysilanes and ethoxypropylsilanes is somewhat hindered[127,128]. The rotation about the Si—O bond is probably only relatively free even in methoxysilanes[128]. A small energy barrier to rotation exists in all alkoxysilanes, but it is not large enough for the estimation of the restriction of free rotation from the dipole moments.

The dipole moments of silanediols show that the internal rotation of the two hydroxy-groups is hindered and that the molecular configuration with an SiOSi angle of 102° is preferred[116].

The high dipole moments of silatranes, which greatly exceed the values calculated without taking into account the donor—acceptor interaction between the silicon and nitrogen atoms[132,135], demonstrate the existence of a transannular N → Si bond.

The dielectric constants ϵ of linear siloxanes are somewhat higher than those of cyclic compounds[139]. The dipole moments of hexa-alkyldisiloxanes are close to that of benzene (2.28). With increase of molecular weight, $\epsilon_{20°}$ increases from 2.18 for hexamethyldisiloxane to 2.79 for $Me_3SiO[SiO(Me)_2]_{300}SiMe_3$ and from 2.39 for D_4 to 2.74 for D_8.[139] Polydimethylsiloxanes with viscosities ranging from 30 000 to 1 000 000 cS have almost identical dielectric constants (ϵ = 2.63 – 2.77).[139] The dielectric constants of polydimethylsiloxanes decrease with increase of temperature and remain virtually constant when the frequency is raised to 10^8 Hz.[139] When the methyl groups at the silicon atoms in cyclodimethylsiloxanes are replaced by polar groups [$F_3CCH_2CH_2$ or $NC(CH_2)_n$ with n = 1 –3], ϵ increases by a factor of 2—4.[87,114] Nevertheless, the dielectric constants of even the most polar cyclosiloxanes, containing CH_2CN groups at the silicon atoms, do not exceed 10,[112] while ϵ_{MeCN} = 37.5.

III. SPECTROSCOPIC CHARACTERISTICS OF THE SILOXANE BOND

1. Vibrational Spectra. The Force Constants and Bond Order

The number of publications devoted to the vibrational spectra of silicon compounds containing siloxane bonds is extremely large. The results of spectroscopic

¶ F = $CF_3CH_2CH_2(Me)SiO$, P = $CH_3CH_2CH_2MeSiO$, and A = PhMeSiO.

† The Si—O bond refraction (1.751 ml mole^{-1}) [138] is much greater than that of the C—O bond in ethers (1.51 ml mole^{-1}).

studies have been summarised in a series of reviews and monographs[57,61,140-149], the most thorough consideration having been given to silicates[61,146]. In this section only the most general features of the vibrational spectra of organosilicon compounds containing Si—O bonds are briefly considered.

Owing to the appreciable ionic character of the siloxane bond, the intensities of the bands and lines due to its vibrations are several times greater than those corresponding to the C—O bond[144,150]. As a result of the strengthening of the Si—O bond due to the $(p \rightarrow d)\pi$ interaction[6-15], the C—O—C and Si—O—Si groups absorb in virtually the same region, despite the greater mass of the atoms in the latter[144,151].

Although the problem of the spectroscopic characteristics of the siloxane bond has attracted the attention of investigators for a long time, it has not so far been possible to calculate theoretically the vibrational spectra of even the simplest compounds containing this bond[61,152,153]. This situation makes it difficult to interpret the spectra and leads to errors (sometimes fairly considerable) in the calculation of the dynamic interaction coefficients K_q, the force constants K_c‡, and the bond orders. Bearing also in mind that there are different approaches to the calculation of the latter parameter[110,154,155], the literature values of the Si—O bond order should be used with some caution.

The fundamental vibrations of the Si—O—Si disiloxane group lie in the following ranges: 450 — 630 cm^{-1} (symmetric vibrations, ν_s) and 930—1170 cm^{-1} (antisymmetric vibrations, ν_{as}). Intense bands in the infrared spectra§ and weak lines in the Raman spectra correspond to the ν_{as} wavenumbers with the opposite relation for the ν_s wavenumbers[140,162,179]. The assignment of the bands and lines corresponding to other vibrations of the siloxane bond is possible only in the simplest cases and is not often encountered in the literature. For example, it has been suggested that the 35 cm^{-1} wavenumber in the infrared spectrum of D_3 corresponds to the $\delta_\perp$ (SiOSi) out-of-plane deformation vibrations[180]. In the far infrared spectra of the higher cyclosiloxanes D_n the $\delta_\perp$ band is displaced towards higher wavenumbers: 50—70 cm^{-1} (n = 4), 80 cm^{-1} (n = 5), 80 and 100 cm^{-1} (n = 6), and 100 and 120 cm^{-1} (n = 7). The $\delta_\perp$ band of hexamethyldisiloxane has been found at 130 cm^{-1} [180] (at 69—86 cm^{-1} in the Raman spectrum) [181]¶.

In the vast majority of spectroscopic studies only antisymmetric Si—O bond vibrations are quoted and discussed. The infrared spectra of disiloxanes, cyclosiloxanes (Table 3), linear[151,182,188,212,214] and branched[211,213,215] siloxanes, silsesquioxanes[201], carbacyclosiloxanes[216], and cyclosiloxazanes[217] contain at least one intense ν_{as} band, the position of which depends more on the structure of the siloxane than on the nature of the substituents at the silicon atom. In the spectra of cyclosiloxanes with a strained ring the band is displaced towards lower wavenumbers. The minimum ν_{as} (Si—O) wavenumber (930 cm^{-1}) has been observed in the infrared spectra of carbacyclosiloxanes with the most strained five-membered ring[216]. In the spectra of cyclotrisiloxanes and six- and seven-membered carbacyclosiloxanes the band is in the region 990—1030 cm^{-1}, [216] and in the spectra of relatively unstrained cyclotetrasiloxanes and eight-membered carbacyclosiloxanes it is displaced towards still shorter wavelengths (1060—1090 cm^{-1}). Estimates of the force constants and bond orders have confirmed that the siloxane bonds in strained rings are appreciably weakened[149,195]. The vibrational spectra of cyclosiloxanes demonstrate the additivity of the intensities, which is probably due to the compensation of the $(p \rightarrow d)\pi$ interaction of the adjacent siloxane bonds[120].

Table 3. The characteristic absorption bands of the Si—O bond in the infrared spectra of siloxanes.

Formula	ν_s, cm^{-1}	ν_{as}, cm^{-1}	References *py*
1	2	3	4
$(H_3Si)_2O$	—	1100	171, 185
$(D_3Si)_2O$(gas)	—	1094	171
$[Me_3SiH]_2O$	550	1058	57, 142, 171
$(Me_3Si)_2O$	516	1053	57, 162, 171, 172, 175, 181, 187—191
$[(CD_3)_3Si]_2O$	461	1060	181
$[(C_nH_{2n+1})_3Si]_2O$ $n=2-4$	—	1069	142, 186, 191, 192
$[Ph(Me)_2Si]_2O$	560	1063	57, 142, 171, 190
$(Ph_3Si)_2O$	—	1075	171, 191, 193
$[CH_2{=}CH(Me)_2Si]_2O$	522	1056	142, 194
$[ClCH_2(Me)_2Si]_2O$	521	1069	57
$[Cl_2CH(Me)_2Si]_2O$	578	1085	57, 142
$[F(Me)_2Si]_2O$	550	1084	142, 194
$[Cl(Me)_2Si]_2O$	578	1070	57, 142, 171, 195
$[I(Me)_2Si]_2O$	551	1068	142, 194
$[Cl_2(Me)Si]_2O$	638	1075	57
$(Cl_3Si)_2O$	718	1170	166, 185, 196
$(Br_3Si)_2O$	693	1094	197
$[HO(Me)_2Si]_2O$	555	1073	57, 171, 172, 195
$[OH(Ph)_2Si]_2O$	—	1078	171
$[MO(Me)_2Si]_2O$			198
M-Li	565, 537	1055, 1022	198
M-Na	551	1010, 1000	198
M-K	539	998	198
$[(MeO)_3Si]_2O$	577	808, 838	199, 200
$Me_3Si[OSi(Me)_2]_nOSiMe_3$		1090	
n=1	—	1050, 1083	150, 151, 188
n=2	—	1039, 1076	151
n=3	—	1034, 1066	151
n=4	—	1057, 1085	151
n=300 ~7000	—	1020, 1090	182
$[H(Et)SiO]_3$	—	1023	205, 206
$(Me_2SiO)_3$	607	1020	150, 180, 183, 201—204
$[Me(C_nH_{2n+1})SiO]_3$ (n=6—10)	—	1015—1025	207
$[Me(Ph)SiO]_3$	532	1018	193
$(Ph_2SiO)_3$	—	1015, 1032	201
$[Et(EtO)SiO]_3$	—	1023	206, 208
$(H_2SiO)_4$	593	1114	209
$[H(Me)SiO]_4$	578	1090	209
$[H(Et)SiO]_4$	—	1085	205
$(Me_2SiO)_4$	555	1078	150, 201, 209, 210
$[Me(Ph)SiO]_4$	510, 530	1085	193
$(Ph_2SiO)_4$	—	1070	201
$[H(Et)SiO]_5$	—	1089	205
$(Me_2SiO)_5$	488, 553	1083	150, 201, 210
$[H(Et)SiO]_6$	—	1086	205
$(Me_2SiO)_6$	496, 552, 591, 638	1070, 1090	150, 201, 210
$(Me_2SiO)_7$	—	1060, 1090	150, 201

*The numbers of the references quoting the tabulated absorption band wavenumbers are underlined.

The nature of the substituents at the silicon atoms has little influence on the position of the ν_{as} band of the SiO(Si) bond in the spectra of cyclosiloxanes. Only when the methyl groups in D_4 are substituted by hydrogen atoms is it displaced towards shorter wavelengths[209,211] (Table 3),

‡ The values of K_q, and K_c have been quoted in a number of publications[18,142,143,150,154-178].

§ In the infrared spectra of linear and cyclic siloxanes more than 50% of the intensity corresponds to the contribution by the antisymmetric vibrations of the Si—O bonds[182]. The intensity of the ν_{as} vibrations of the Si—O bonds in linear disiloxanes is approximately 10 times greater than the ν_s intensity[183].

¶ Infrared spectra of disiloxanes in the range from 30 to 100 cm^{-1} have been published also by Robinson and Lafferty[184].

while in linear siloxanes such a shift is not observed[142, 211-213]. In the infrared spectra of linear[140,151,182,188,212,214] and branched[213,215] siloxanes and also cyclosiloxanes containing more than four siloxane units (Table 3) the ν_{as}[Si—O(Si)] band is split into two (or more) components. In the spectra of cyclodimethylsiloxanes, starting with D_4, the shift of the absorption maxima towards higher wavenumbers with increase in ring size is relatively small (20—30 cm^{-1}). The spectra of linear polydimethylsiloxanes $Me_3Si[OSiMe_2]_nOSiMe_3$ showed two bands with maxima in the wavenumber ranges 1034—1057 cm^{-1} and 1066—1085 cm^{-1} (n = 1—4) [151] and at 1020 and 1090 cm^{-1} (n = 300—7000) [182] (Table 3). The ν_{as}(Si—O) absorption maxima in the spectra of branched siloxanes have been recorded at 1040 and 1110 cm^{-1}.[211,213,215] In the infrared spectra of the majority of cyclosiloxazanes two bands due to the ν_{as} vibrations of the Si—O bond are also observed. In the spectra of compounds with a six-membered ring these bands are displaced towards longer wavelengths, which probably indicates the strain of the siloxazane ring[217].

The position of the ν_s(SiO) band in the spectra of silsesquioxanes with organic substituents is the same as in the SiO_2 spectrum (an intense broad band in the region of 500 cm^{-1}).[218] In the spectra of the octamers $(RSiO_{1.5})_8$, 3—4 maxima are observed and in the spectra of the hexamers $(RSiO_{1.5})_6$ between 6 and 8 maxima at 360—660 cm^{-1}.[141,219]

In contrast to cyclosiloxanes, the positions of the ν_s(SiO) and ν_{as}(SiO) bands in the spectra of disiloxanes depend to a large extent on the nature of the substituents at the silicon atoms. With increase of the electronegativity of the substituents (in particular following the substitution of the methyl groups in hexamethyldisiloxane by hydrogen or halogen atoms and phenyl or hydroxy-groups) the ν_s(SiOSi) and ν_{as}(SiOSi) bands are displaced towards higher wavenumbers (Table 3). Thus, on passing from hexamethyldisiloxane to disiloxane and to hexachlorodisiloxane, the ν_{as}(SiOSi) change from 1060 to 1100 and 1170 cm^{-1} respectively[185]. The force constants of the Si—O bond calculated from the spectroscopic characteristics of these three compounds are 6.96×10^{-6}, 8.17×10^{-6}, and 9.18×10^{-6} cm^{-2} and the bond orders are 1.13, 1.33, and 1.49 respectively[165]. The main cause of the strengthening of the siloxane bond with increased electronegativity of the substituents at the silicon atoms is believed to be the enhancement of the $(p \rightarrow d)\pi$ interaction due to the increase of the positive charge at the silicon atom[142,149,158,160,164-166,175,185,220].

In the spectra of alkali metals tetramethyldisiloxane-1,3-diolates $(MOMe_2Si)_2O$ (M = Li, Na, or K) the ν_{as}(SiOM) bands are displaced towards higher wavenumbers relative to the ν_{as}(SiOH) band in the spectrum of $(HOMe_2Si)_2O$ (910 cm^{-1}): 980 cm^{-1} (for M = Li), 963 cm^{-1} (for M = Na), and 941 cm^{-1} (for M = K),[198] while the ν_{as}(SiOSi) bands undergo the opposite shift towards lower wavenumbers (Table 3). This shows that, together with the increase of the force constant of the SiO(M) bond on passing from M = H to M = K, the Si—O(Si) bonds are weakened[198].

The Si—O(C) bond in alkoxysilanes is much weaker than the Si—O(Si) bond in siloxanes. The ν_s(SiOC) wavenumber occurs in a shorter wavelength region (700—850 cm^{-1}) than the ν_s(SiOSi) wavenumber[143,148,149,158,162,173,185,192,221].

As a result, the splitting of the Si—O stretching vibration bands into ν_s and ν_{as} in the spectra of alkoxysilanes is much less marked (about 200 cm^{-1}) than for siloxanes (about 500 cm^{-1}). This is associated both with the breakdown of the symmetry in the electronic configuration of oxygen and with the change of the angle between its valence bonds[162].

On passing from hexamethyldisiloxane to methoxytrimethylsilane, the coefficient of dynamic interaction diminishes from 6.96×10^{-6} to 6.17×10^{-6} cm^{-2}.[158,165] The order of the siloxane bond in tetramethoxysilane is unity, because its force constant in this case virtually coincides with the calculated constant for a "single" Si—O bond[177]. The order of the siloxane bond in alkoxyalkylsilane molecules is also close to unity[143,155,165]. On passing from n = 1 to n = 4, there is a linear growth of the intensity of the ν_{as}(SiOC) band in the spectra of the compounds $Me_{4-n}Si(OEt)_n$.[221]

When the methyl groups in methoxytrimethylsilane are substituted successively by chlorine atoms, the ν_{as}(SiOC) band shifts towards shorter wavelengths (from 720 cm^{-1} for Me_3SiOMe to 810 cm^{-1} for Cl_3SiOMe),[158,222,223] while the force constant increases correspondingly from 6.17×10^6 cm^{-2} to 8.23×10^6 cm^{-2}.[158]

This change is proportional to the increase of the force constant on passing from $(Me_3Si)_2O$ to $(Cl_3Si)_2O$. The shift of the ν_{as}(SiOC) band towards higher wavenumbers† is observed also when hydrogen atoms are replaced by chlorine in tetraethoxysilane[227].

Thus, as in disiloxanes, highly electronegative substituents at the silicon atom in alkoxysilanes also cause an appreciable increase in the Si—O bond order. The effect of the $(p \rightarrow d)\pi$ interaction plays a decisive role in this phenomenon[142,149,153,158,160,162,165,224,225]. The occurrence of this effect in methylmethoxysilanes probably has a significant influence also on the nature of the Si—C bonds, namely it leads to their weakening and a decrease of their covalent character[179].

Apart from the corresponding ν_s(Si—O) and ν_{as}(Si—O) lines the tetramethoxysilane spectrum shows an intense polarised line at 640 cm^{-1}, probably due to the fully symmetrical stretching vibrations of the SiO_4 tetrahedron[199,200].

An intense absorption in the region of 1000—1200 cm^{-1}, due to the stretching vibrations of the C—O bonds, is observed in the spectra of all alkoxysilanes and alkoxysiloxanes[153,156,158,167,174,177-179,191,208,221-223,226-244]. This absorption region is extremely stable and depends little on the nature of the substituents at the silicon atoms[153,221,222,227,245].

In the infrared spectra of the silatranes $RSi(OCH_2CH_2)_3N$, containing a pentacoordinate silicon atom, the absorption band due to the C—O bond is in the region of 1100 cm^{-1}.[246] In the spectra of vinyloxy-, phenoxy-, and acetoxy-silanes, where the C—O bond order is enhanced, this band is located at 1180, 1250—1280, and 1200—1270 cm^{-1} respectively[249-251].

Comparison of the vibrational spectra of siloxanes, silanols, and siloxanols containing analogous substituents at the silicon atom shows that the siloxane bond in the SiO(H) group is only a little weaker than in the SiO(Si)

† A slight shift of the ν_{as}(Si—OC) band is observed also when a halogen atom, an alkyl group, a phenyl group, and an alkoxy- or acetoxy-group are introduced in the p-position of the trimethylphenoxysilane ring, which indicates some change in electron density at the silicon and oxygen atoms, but these shifts are too small to yield a correlation[247]. The position of the ν_{as}(Si—OC) band depends little on the nature and position of the substituent in the benzene ring of phenoxychlorosilanes[168,248].

group[158,163,171,172,175]. For example, the force constant of Si—O bond in Me_3SiOH and Me_3SiOD is $K^* = 6.92 \times 10^6$ cm^{-2}, while in $(Me_3Si)_2O$ it is $K^* = 6.96 \times 10^6$ cm^{-2}.[158,163] When silanols are associated via hydrogen bonding, the Si—O(H) bonds are strengthened still more[149,252,253]. Association of silanol molecules shifts also the split ν_{as}[SiO(H)] bands. Thus the infrared spectrum of triethylsilanol shows maxima at 841 and 828 cm^{-1}.[254]

Very intense ν(SiO) absorption bands are observed in the infrared spectra of alkali metals trimethylsilanolates in the range 900—1000 cm^{-1}.[57,158,198] As was to be expected, high force constants indicate an appreciable strengthening of the Si—O(M) bond (M = alkali metal) relative to the Si—O(H) [163,198] or Si—O(Si) [57] bonds. Thus the order of the siloxane bond in Me_3SiONa is 25% higher than in Me_3SiOH and 40% higher than in Me_3SiOMe.[163]

The absorption band characteristic of the SiO—M bond in the infrared spectra of the products of the interaction of $(EtO)_4Si$ with lithium, sodium, potassium, and magnesium, and other metal acetates in an aqueous alcoholic medium shifts towards a longer wavelength with increase of the atomic weight of the metal[255]. The assignment of the ν(SiO) and ν(MO) bond vibrations in the spectra of siloxane derivatives of the elements with organic substituents is usually difficult. So far only ν[SiO(M)] absorption bands have been identified (M is a Group III—VI or VIII element) and these occur as a rule in the range 800—1100 cm^{-1}.[231,256-290]

In the infrared spectra of organosilicon peroxides $R_3SiOOSiR_3$ (R = Me or Et) and also $Me_3SiOOCMe_3$ the bands in the range 750—770 cm^{-1} have been assigned to the symmetric vibrations of the Si—O bond and those at 146 and 175—185 cm^{-1} to the deformation vibrations of this bond[291-293].

2. NMR Spectra

Only the ^{29}Si isotope, which has a magnetic moment ($I = 1/2$), can be used for a direct investigation of the siloxane bond by NMR. Studies on the ^{29}Si chemical shifts, which require a special technique owing to the relatively low natural abundance of this isotope (4.7%) and the low sensitivity of ^{29}Si NMR spectroscopy[294], have so far been extremely limited in scope[295-307]. The chemical shifts in the ^{29}Si and ^{13}C NMR spectra of related silicon and carbon compounds vary in the opposite sequences. The $\delta(^{29}Si)$ chemical shifts vary within wide limits depending on the number of siloxane bonds and the nature of the substituents at the silicon atom. Selected data are presented in Table 4.

The shifts $\delta(^{29}Si)$ for silicon atoms forming a single bond with oxygen are positive (the region of the lowest fields relative to Me_4Si), increasing with increase of the electronegativity of the substituents linked to the oxygen atom. For trimethylsilyl esters of organic and inorganic acids, an almost linear relation is observed between $\delta(^{29}Si)$ and the pK_a of the corresponding acids[299,305]. For silicon linked to two and more oxygen atoms, the $\delta(^{29}Si)$ are negative—with the exception of the acyloxysilanes[303]. The absolute values of the chemical shifts increase steadily with increase of the number of siloxane bonds at the silicon atoms [$\delta(^{29}Si)$ = −113.0—109.0 for quartz].[303] Presumably the increase of the chemical shift in the above sequence is due to the overall transfer of π-electron density at the oxygen atoms to silicon via the $(p \rightarrow d)_\pi$ coupling mechanism[302]. For polydimethylsiloxanes and cyclodimethylsiloxanes D_n (n = 4—6), the $\delta(^{29}Si)$ are in the range between −23.0 and −19.7 p.p.m.; for D_3, the signal is displaced towards lower fields (−9.9 p.p.m.).[302] Thus the ^{29}Si NMR method, like other physical procedures, reveals a significant difference between the state of the silicon atoms forming part of the strained planar cyclotrisiloxane molecule and the silicon atoms in any other unstrained structures. For linear oligomers MD_nM (M = Me_3Si, D = Me_2SiO, n = 0–6), the $\delta(^{29}Si)$ corresponding to the silicon atoms in the M and D fragments change slightly on passing from n = 0 and 1 to n = 3 and then remain constant[302].

Table 4. The chemical shifts in the ^{29}Si NMR spectra of compounds containing the siloxane bond.

Compound	δ, p.p.m.	References
$(Me_3Si)_2O$	6.3	298, 302
$(Et_3Si)_2O$	9.1	301
$(Me_3Si^*O)_2Si^{**}Me_2$	6.1 (*)	302
	−22.1 (**)	
$(Me_3Si^*O)_3Si^{**}Me_2$	6.7 (*)	302
$(Me_3Si^*O)_4Si^{**}$	−65.0 (**)	
	8.0 (*)	302
	−105.2 (**)	
SiO_2	−113—109	302
$(Me_2SiO)_n$ n=3	−9.2	302
n=4	−20.0	302
n=5	−22.8	302
n=6	−23.0	302
$Me_3Si^*O[Si^{**}(Me)_2O]Si^*Me_3$ n=1	6.1 (*)	302
	−22.1 (**)	
n=2	6.7 (*)	302
	−22.3 (**)	
n=3	6.5 (*)	302
	−22.4 (**)	
Me_3SiOMe	17.2	302, 306
$Me_2Si(OMe)_2$	−2.5	302, 306
$MeSi(OMe)_3$	−41.4	302, 306
$(MeO)_4Si$	−79.2	302, 306
$(Me_3SiO)_3B$	12.3	305
$(Me_3SiO)_3PO$	20.0	305
$Me_3SiOCOMe$	22.0	305, 306
$Me_3SiOCOCF_3$	33.2	305
$(Me_3SiO)_2SO_2$	33.7	305
$Me_3SiOSO_2CF_3$	44.6	305
$Me_2Si(OCOMe)_2$	7.0	303
$Me_2Si(OCOCF_3)_2$	−14.0	303
$Ph_2Si(OH)_2$	−31.7	303

Data for the spin—spin interaction constants J between a hydrogen atom and a silicon atom, also involved in bonding with oxygen atoms are relatively few; $J(^{29}Si—H)$,[308-318] $J(^{29}Si—C—H)$,[312,319,320] and $J(^{29}Si—O—C—H)$ [312,319] have been determined. The attempt to trace a correlation between the $J(^{29}SiH)$ and the number of substituents X in the molecules of the $X_{4-n}SiH_n$ series in accordance with the equation

$$J(X_{4-n}SiH_n) = J(SiH_4) + (4-n)\,[J(SiH_3X) - J(SiH_4)]$$

was unsuccessful[311,313]. The greatest deviations from the linear relation were observed for compounds with the most electronegative substituents (X = OR, F, or Cl) like, incidentally, the deviations from the analogous $J(^{13}CH)$ relation for the corresponding carbon compounds[321-323]. The deviations have been explained by the appreciable polarisation of the carbon or silicon atom in these compounds[311,313].

The general equation, which is more suitable for the calculation of $J(^{29}SiH)$ and $J(^{13}CH)$ for compounds of the type HMXYZ (M = C or Si) takes into account the pair interactions of the substituents:

$$J(HMXYZ) = J(MH_4) + A(\alpha_x+\alpha_y+\alpha_z) + B(\alpha_x^2+\alpha_y^2+\alpha_z^2) + C(\alpha_x\alpha_y+\alpha_y\alpha_z+\alpha_z\alpha_x).$$

The maximum deviations of the calculated J from the experimental values do not exceed 6—9 Hz. For M = Si, we have A = 18.26 Hz eV^{-2}, B = 1.78 Hz eV^{-2}, and C = −2.98 Hz eV^{-2}. The parameters α, which constitute a measure of the effective electronegativities of the corresponding substituents, can be determined by means of the above equation from the J for the compounds MH_3X, MH_2X_2, etc. For silicon derivatives, α_X = −1.49 eV when X = OMe, and α_X = −1.76 eV when X = $OSiH_3$.[310] The values of α_X for the series of compounds with M = Si are always smaller than for the corresponding compounds with M = C. This may be due to the higher polarisability of the silicon atom in relation to carbon and at any rate provides no grounds for the interpretation of the experimental findings by taking into account the possibility of π bonding in the silicon compound.

Numerous compounds containing the siloxane bond have been investigated by ^{1}H NMR. Some of the results obtained have been described in other sections and have been examined in another review[324]. Many factors which are difficult to take into account and which influence the proton chemical shift hinder the analysis on the basis of ^{1}H NMR data of the changes in electron density at the silicon and oxygen atoms joined directly. Nevertheless ^{1}H NMR spectroscopy can be used successfully to refine ideas on the nature of the siloxane bond. Systematic studies by ^{1}H NMR on siloxanes[302,325-330], heterosiloxanes[274,276,279,280,331,332], and alkoxysilanes[312,319,333-337] confirm the significant role of π bonding in the structure of these molecules. It has been shown for oligomeric siloxanes of the type $Me_2(X)SiO[Si(Me)_2O]_nSi(X)Me_2$, where X = Me, H, Cl, or $ClCH_2$ and n = 0—6, that the influence of the substituent X can be transmitted through the chain via two or even three siloxane bonds[326]. Relations of the type

$$\tau_i(OCH_2) \text{ or } \tau_i(OCCH_3) = a + b\Sigma\sigma_i^*,$$

(σ^* are the inductive Taft constants for the substituents R), in which the parameter b diminishes with increase of the number n, have been found for the ethoxysilanes $R_{4-n}Si(OEt)_n$.[334] A similar tendency, characterising the decreased ability of the silicon atom to transmit the inductive effect of the substituents to the adjoining bonds with increase of the number of Si—O bonds in the molecule, has also been observed by kinetic methods[338] and by infrared spectroscopy[339] for compounds of different classes. Thus the phenomenon is probably general.

3. Electronic Spectra

Liquid polydimethylsiloxanes are transparent in the visible and near ultraviolet regions. In the range 246—270 nm a number of absorption bands have been observed in the ultraviolet spectra of linear and cyclic polydimethyl- or polymethylphenyl-siloxanes[340].

The attachment of an oxygen atom to a silicon atom linked to a vinyl[341], phenyl[342], or pentafluorophenyl[342] group does not have a significant influence on the absorption of these groups. The λ_{max} for the vinyl group in the ultraviolet spectra of linear and cyclic siloxanes are in the same range (178—180 nm) as for trialkylvinylsilanes and are independent of the number of oxygen atoms joined to the Si—CH=CH_2 group[341].

A bathochromic shift of the absorption band due to the phenyl group relative to the analogous carbon derivatives has been observed in the ultraviolet spectra of methylphenoxysilanes[225]. The position of the absorption maximum of the phenyl group in methylphenoxysilanes $Me_nSi(OPh)_{4-n}$ (n = 1—4) is independent of the number of phenoxy-groups[225,343,344].

The ultraviolet spectra of alkoxy- and trialkylsiloxybenzenes[225,343-345] or their complexes with tetracyanoethylene[345] and the results of quantum-chemical calculations[345] on the structure of phenoxy-derivatives of silicon indicate the occurrence of the $(p \rightarrow d)_\pi$ interaction between the oxygen and silicon atoms.

IV. PHYSICAL PROPERTIES AND MOLECULAR STRUCTURES OF POLYSILOXANES

Owing to the weak intermolecular interaction, the surface tension of polydiorganosiloxanes (particularly polydimethylsiloxanes) is much lower than that of the usual organic liquids with the same densities and boiling points[346,347]. In the series of linear polydimethylsiloxanes it increases from 15 dynes cm^{-1} for hexamethyldisiloxane to 22 dynes cm^{-1} for the polydimethylsiloxane oil with a viscosity of 10^5 cP.[139,347,348] The surface tensions of cyclodimethylsiloxanes D_n (n = 3—7) increase with increase of ring size from 17.3 to 18.3 dynes cm^{-1} at 25°C.[349] The surface tensions of mixtures of polyorganosiloxanes are additive[346].

A relatively high compressibility, which decreases with increase of molecular weight approaching an asymptotic value, is characteristic of the lower polydimethylsiloxanes[350]. With increase of pressure, the compressibility of polydimethylsiloxanes increases more slowly than that of hydrocarbons. At pressures of about 1000 kgf cm^{-2} the compressibility of polydimethylsiloxanes is higher than that of dodecane but at 40 000 kgf cm^{-2} it is lower[350]. At a pressure of 35 000 kgf cm^{-2} high-molecular-weight polydimethylsiloxane does not crystallise[351]. When the methyl groups in the polydimethylsiloxane are replaced by higher alkyl groups, the compressibility gradually falls with increase of the size of the substituent, increasing after substitution by hydrogen atoms[139].

The boiling points as well as the heats of evaporation of the linear polydimethylsiloxane $M_3D_nM_3$, where n = 1—6, and cyclodimethylsiloxanes D_m (m = 3—8) are lower than those of the alkanes having the same molecular weight[139,348]. With increase of n by unity, the heat of evaporation of polydimethylsiloxane increases by only 960 cal mole^{-1}.

With increase of molecular weight, the boiling points of polydimethylsiloxanes increase more slowly than in the case of n-alkanes.

The heat capacities of dimethylsiloxane polymers with a viscosity of 0.65—1000 cS (0.32 – 0.35 cal g^{-1} deg^{-1}) are somewhat lower than those of the corresponding hydrocarbons[139].

The viscosities of low-molecular-weight linear and cyclic polydiorganosiloxanes are somewhat lower than those of hydrocarbons with comparable molecular weights[348,349]. The activation energies for the viscous flow of siloxanes are also lower than for hydrocarbons. The activation energy amounts to 3.8 kcal mole^{-1} for

polydimethylsiloxanes[352], to 5.41 kcal mole^{-1} for siloxane polymers with tetramethylene units in the main chain[353],

$$Me_3SiO[Si(Me)_2(CH_2)_4Si(Me)_2O]_nSiMe_3-$$

and to 6—7 kcal mole^{-1} for saturated hydrocarbons[353]. The average length of the flow segment of high-molecular-weight polydimethylsiloxane corresponds to 7.2 siloxane units[352], while the length of the similar segment for long hydrocarbon chains corresponds to 20—25 units[354].

When the methyl groups in polydimethylsiloxane are replaced by the polar chloromethyl[355], phenyl[108], or chlorophenyl[356] groups, the activation energy for the viscous flow increases, amounting to 4.3 kcal mole^{-1} for polymethylpropylsiloxane, 7.9 kcal mole^{-1} for polymethyl-3,3,3-trifluoropropylsiloxane, and 11.9 kcal mole^{-1} for polymethylphenylsiloxane[357].

With increase of pressure, the viscosity of polydiorganosiloxanes increases more than that of hydrocarbons[358]. With increase of shear rate, the viscosity of polysiloxanes diminishes and at high shear rates the temperature variation of the viscosity becomes insignificant[359].

The low temperature coefficients of the viscosity of polydimethylsiloxanes[108,350,352,353,359] and the decrease of their viscosity with increase of shear rate show that siloxane molecules have a coiled conformation. Indeed the structure of the coiled siloxane molecule with the alkyl groups "sticking out" is responsible for the insignificant molecular interaction, as a result of which the viscosity is also relatively low. With increase of temperature, the molecules uncoil and the intermolecular interaction becomes more intense, which leads to an increased viscosity, partially compensating its usual decrease with temperature. As a result, the temperature coefficient of the viscosity of polymethylsiloxane is much lower than for hydrocarbons.

The coiling of the siloxane chain is probably the cause of the greater deviation of the heats of mixing of polydimethylsiloxanes with benzene from the theoretical values[360].

Indeed the siloxane chain in the polydimethylsiloxane film on the surface of water at 20°C is coiled into a helix containing six monomeric units per turn[347]. With increase of temperature, the length of the turn of the helix increases. Substitution of methyl groups by phenyl groups reduces the tendency of the siloxane chain to coil up[108,347]. This tendency is manifested to an even greater extent when methyl groups are replaced by ethyl groups[347].

The helical shape of the siloxane molecule (Fig. 2) has also been established by electron diffraction[361] and X-ray diffraction[21] methods. An X-ray diffraction study of extended polydimethylsiloxane raw rubber[21] and the finished rubber obtained from it[22] showed that there are six siloxane bonds in the monoclinic cell with the parameters (Å) $a = 13.0$, $b = 8.3$, $c = 7.75$, and $\beta = 120°$. In the polydimethylsiloxane molecule the *trans*-configuration is preferred to the *gauche*-configuration[362,363].

The coiling of the siloxane molecule into a helix has been explained[362,364] by the tendency of the weak Si—O dipoles to undergo intramolecular compensation as a result of which each Si—O dipole is associated with a dipole having the opposite orientation (O—Si). The intramolecular compensation of the individual dipoles has been confirmed by the insignificant change of the dipole moment with increase of the molecular weight of polydiorganosiloxanes.

Bearing in mind the polarity of the Si—O bond, many physical properties of polydiorganosiloxanes (the fact that they are hydrophobic, their compressibility, surface properties, etc.) can be explained solely in terms of the helical macromolecular structure forming a "coil" with "protruding" hydrocarbon groups[139,347,350,360]. However, one should not forget that the effect of the $(p \rightarrow d)_\pi$ bonding in the Si—O—Si system should also weaken the intermolecular interaction.

According to ^{1}H NMR data, segmental motion, which has been attributed to chain drift, takes place in polydimethylsiloxane even at very low temperatures (−136°C).[365-372] The segmental mobility of polydimethylsiloxane raw rubber is much higher than that of natural raw rubber[373]. Comparison of the dielectric properties of polydimethylsiloxane with ^{1}H NMR and X-ray diffraction data suggested[365] that motion of the second kind, preceding the onset of chain rotation, occurs in the crystalline polymer appreciably below the melting point of the crystals. The activation energy for the rotation of the polydimethylsiloxane chain calculated from the ^{1}H NMR data is 8 J mole^{-1}.[365]

The methyl groups in polydimethylsiloxanes rotate unusually readily about the Si—O bonds even at 196°C.[368-371]‡ Such rotation of the methyl groups is probably one cause of the increased distances between the macrochains and of the weakened intermolecular interaction in polydimethylsiloxanes[370]. On the other hand, the rotation of the phenyl groups at low temperatures is fully hindered and even at room temperature their rotation is somewhat retarded[371]. The consequences of the ease of rotation of the methyl groups is the high molar volume and the low density of the cohesion energy[139,350] of polydimethylsiloxane. The average molar volume of the Me_2SiO unit is 75.5 ml mole^{-1}.[374] The low density of the cohesion energy of polydimethylsiloxane, which is appreciably lower than for other polymers, is in fact responsible for the low boiling points, low heats of evaporation, low surface tensions, high compressibilities and low dielectric constants of liquid polydimethylsiloxanes and also for the low heats of fusion and moderate adhesion [energy] of high-molecular-weight polydimethylsiloxanes.

The weakness of the intermolecular forces is also manifested in a number of other properties of polydimethylsiloxanes. The lower ultrasonic velocities in polydimethylsiloxanes compared with the majority of organic liquids having similar densities[139,375,376] indicate a loose packing and a weak intermolecular interaction of the siloxane molecules.

Polydimethylsiloxane becomes rubber-like only when its molecular weight is fairly high (about 10^6) and when its molecular weight is 4×10^5 it flows in the cold although it remains solid. In contrast to other types of raw rubber, unfilled vulcanised polydimethylsiloxane specimens have a very low strength (2—5 kgf cm^{-2}).[377] A characteristic feature of siloxane raw rubbers is also an appreciably smaller decrease of strength with increase of temperature than for other elastomers[377].

Among all the known elastomers, polydimethylsiloxane raw rubber has the lowest glass point (−123°C).[378] The high rate of crystallisation of polydimethylsiloxane raw rubber, which crystallises rapidly at −54°C without supercooling, has also been explained by the weak intermolecular interactions and mobility of the siloxane molecules at low temperatures[379,380].

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‡ The anomalously high mobility of the methyl groups, attributed to the "out-of-plane" deformations of the Si—O—Si bonds, has also been observed in an X-ray diffraction study of structures containing the planar six-membered siloxane ring[25,29].

The substitution of methyl groups in polydimethylsiloxane by vinyl groups does not affect the mobility of the polymeric chains[371]. The introduction of 3,3,3-trifluoropropyl groups has little effect on the molecular motion[371], but the replacement of the dimethylsiloxane units by methylphenylsiloxane[372] or diphenylsiloxane[371] units greatly hinders such motion. On the other hand, the substitution of methyl groups in polydimethylsiloxane by hydrogen atoms increases the mobility of the siloxane chains[372].

Thus the mobility of the polysiloxane molecules decreases in the sequence

$$[H(Me)SiO]_n > [Me_2SiO]_n > [CH_2{=}CH(Me)SiO]_n > [Pr(Me)SiO]_n > [Me(Ph)SiO]_n > [Ph_2SiO]_n.$$

The results of studies on the polysiloxanes by ^{1}H NMR agree well with data for the thermodynamic flexibility of polymeric siloxane molecules obtained in a study of solutions of the polymers by light scattering, osmometry, and viscometry[381-387]. Although the rotation of the polymeric chain about the Si—O bond is restricted to some extent (the unperturbed mean square distance between the ends of the polymeric molecule is much greater than the value calculated theoretically for free rotation), nevertheless the flexibility of the siloxane molecule is much greater than that of other polymeric chains[381-387].

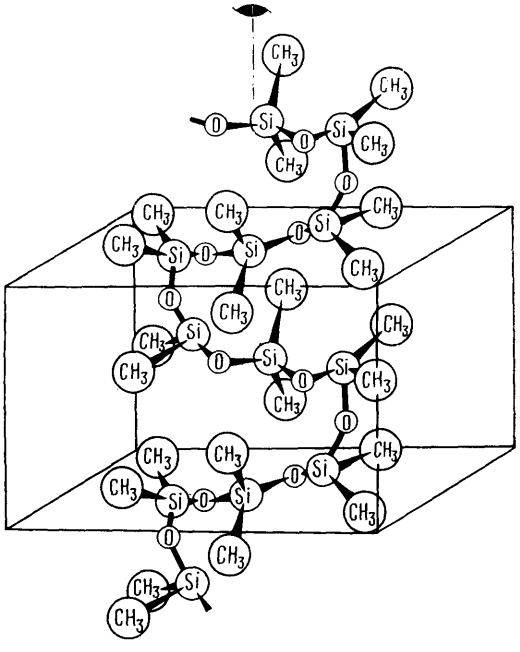

Figure 2. The crystal structure of polydimethylsiloxane[21].

The results of a calorimetric study of the mixing of polydimethylsiloxane with various solvents also led to the conclusion that the molecules of this polymer are very flexible[360,363,364]. This is likewise indicated by the appreciable atomic polarisations P_a and the anomalously short dielectric relaxation times of disiloxanes[99] and cyclosiloxanes[388]. The similarity of the P_a for hexamethyldisiloxane and D_3 [388] demonstrates a significantly lower flexibility of the Si—O bonds in D_3. On the other hand, judging from the value of P_a, the flexibility of the siloxane bonds in the relatively unstrained D_4 ring is much greater and close to their flexibility in linear polydimethylsiloxanes[99].

The great flexibility of the SiOSi angles is responsible for the possibility of the existence of many cyclosiloxanes in the form of several conformers equally probably on energy grounds, which are readily interconverted[28,389,390]. The results of calculations of the overlap integrals of the d and p orbitals for various configurations of siloxane rings agree well with this hypothesis[391].

Two crystalline modifications (orthorhombic and triclinic) and three modifications have been isolated for A$_3$ § and A$_4$ respectively[390].

According to spectroscopic data, only one conformation is possible for dimethylcyclosiloxanes with an odd number of siloxane units ($n > 3$), in which all the silicon atoms are in the same plane and all the oxygen atoms are in another plane parallel to it[392]. When n is even, two (or more) conformations of cyclic siloxanes are possible. The folded D_4 ring can exist in the form of three conformers of different symmetries. One of these is present in the gas and liquid phases[393] and two others in the crystalline state. In the low-temperature modification of D_4, four oxygen atoms and four silicon atoms are located in two separate planes disposed at an angle of 30°.[61] Certain octaorganosilsesquioxanes also exist in the form of two modifications[389].

X-Ray diffraction studies on silicates demonstrate the existence of different equilibrium conformations also in cyclic silicate anions, which is due to the high flexibility of the siloxane chain[61].

Spectroscopic studies and thermodynamic calculations have led to the conclusion that rotation about the Si—O bond in siloxanes is virtually free (the potential barrier does not exceed several tens of kcal mole^{-1}).[9,382,393] Nevertheless rotation about the siloxane bond is apparently always restricted to some extent in all compounds and the energy barrier depends appreciably on the nature of the substituents at the silicon atoms.

The flexibility of the polysiloxane molecule decreases following the substitution of the methyl groups at the silicon atoms by propyl[394], trifluoropropyl[384], or phenyl[384] groups. In the presence of two phenyl groups at the same silicon atom, the flexibility of the siloxane polymer is significantly smaller than that of the methylphenylsiloxane polymer with the same content of phenyl groups.

Thus the thermodynamic flexibility of polymethylphenylsiloxane corresponds to that of the dimethylsiloxane—diphenylsiloxane copolymer containing 25—30 mole % of diphenylsiloxane units[385,386].

The flexibility of the siloxane molecule decreases particularly appreciably on passing from a linear to a "ladder" structure; although the rotational mobilities of the phenyl group in the linear methylphenylsiloxane and the ladder phenylsiloxane $[PhSiO_{1.5}]_n$ polymers are approximately the same, the rigidity of the latter is appreciably greater[395-402]. The number of units (50) in the segment of the ladder phenylsiloxane is ten times greater than in the segment of the methylphenylsiloxane polymer[89,395,401].

The thermodynamic flexibility of polydimethylsiloxane is increased by the introduction of phenylene groups into the siloxane chain[402].

Certain problems of the effect of the nature of the siloxane bond on the properties of oxygen compounds of

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§ A = $C_6H_5(CH_3)SiO$.

silicon, which were not considered here owing to the limited space available, are dealt with in monographs and reviews[56,403-405].

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Nitroacetylenes

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The review examines the methods of synthesis, structures, infrared, ^{1}H NMR, and ultraviolet spectra, and physical and chemical properties of a new class of compounds—nitroacetylenes.
The bibliography includes 83 references.

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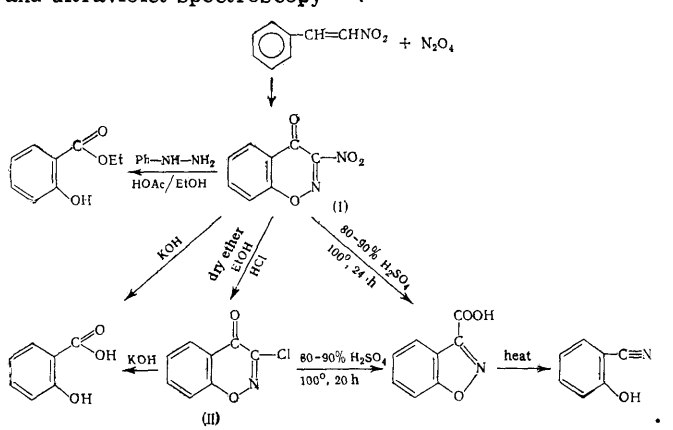
I. INTRODUCTION

Nitroacetylenes constitute a new, still little investigated class of organic compounds which is interesting in view of a combination of the energy-deficient triple bond and the electron-accepting nitro-group. α-Acetylenic nitro-compounds, where the conjugation of the π-electron system with the electrophilic nitro-group leads to extensive possibilities of their employment in organic synthesis, have attracted particular attention.

Whereas extensive data were available as early as 1950 on the methods of synthesis and a wide variety of reactions of ethylenic nitro-compounds, systematic study of acetylenic nitro-compounds did not begin essentially until 1969. This paper surveys the results of studies published until the beginning of 1973.

The first mention of nitroacetylenes dates back to 1903[1] when Wieland obtained by the reaction of nitrogen oxides with cinnamaldehyde a low yield of a yellow crystalline substance having the overall formula $C_8H_4N_2O_4$. On the basis of elemental analysis and the determination of molecular weight, Wieland erroneously attributed to this compound the structure of *p*-nitrophenylnitroacetylene. However, the author did not rule out other possible structures.

p-Nitrophenylnitroacetylene was probably obtained for the first time much later by Novikov et al.[2] by nitrating β-nitrostyrene with nitrogen tetroxide, but attempts to reproduce this reaction were unsuccessful: instead of nitroacetylene, the product isolated was (probably the same as in Wieland's reaction[1]) 1-nitro-2-azachromone (3-nitro-4*H*-1,2-benzoxazin-4-one)[3] (I), whose structure has been demonstrated chemically and by ^{1}H NMR, infrared, and ultraviolet spectroscopy[3-5]:



Later heavy dark-red oils were obtained by the dehydrohalogenation with the aid of amines of 1-bromo-1-nitroalkenes[6] and 1-bromo-1-nitro-2-phenylethylene[7]; the structure of α-nitroacetylenes was attributed to the oils.

Thus, on treatment with diethylamine, 1-bromo-1-nitro-2-phenylethylene was converted into an oil which exploded on distillation, reacted instantly with Baeyer's reagent, and did not decolorise bromine water. The molecular weight and the nitrogen content corresponded to the formula of phenylnitroacetylene. However, these experiments could not be reproduced either[3].

It was not until 1969 that Jäger and Viehe described for the first time a reliable method for the synthesis of t-butylnitroacetylene and its homologues[8]. These investigations were subsequently extended[3].

Among non-conjugated nitroacetylenes, only the hexanitro-derivative has so far been obtained[9].

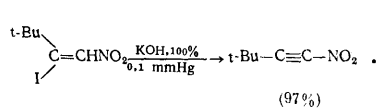
1,1,1,6,6,6-Hexanitrohex-3-yne[9], 1-nitroalk-1-ene-3-ynes[10-13], and a number of nitrobutenyne derivatives of the elements (silicon and germanium)[14] were also obtained recently. Among functional derivatives of nitroacetylenes, only glycols are known[15,16].

II. THE PREPARATION OF NITROACETYLENES

The simplest α-nitroacetylenes were obtained (by analogy with nitroalkenes) by the dehydrohalogenation of halogenonitroalkenes formed as a result of the addition of NO_2X (X = Cl[17-20] or X = I[21]) to acetylenic compounds.

Nitroiodination proved to be most suitable for this purpose. Difficulties arose in the second reaction stage (dehydroiodination), for which various reagents were employed[3]: tertiary amines, sodium acetate in dimethylformamide (DMF), silver oxide in ether, and potassium t-butoxide; the reaction was followed by the intensity of the band due to the triple bond in the infrared spectra of the final product. Potassium hydroxide proved to be the most effective dehydrohalogenating agent.

Thus, by passing 2-iodo-3,3-dimethyl-1-nitrobut-1-ene (III) through a tube with alkali heated to 110-120°C, t-butylnitroacetylene (IV) was obtained (yield 96-97%, purity of the product according to gas-liquid chromatographic data 98-100%):



Nitroacetylenes with isopropyl (V, yield 74%) and n-propyl (VI, yield 28%) groups were obtained similarly. n-Butyl-α-nitroacetylene was isolated from a mixture with the starting material. The formation of phenylnitroacetylene was demonstrated spectroscopically ($\nu C{\equiv}C$ = 2240 cm^{-1}); its low volatility made its further purification difficult[3].

Stereoisomeric mixtures of the initial iodonitroalkenes were usually dehydroiodinated. The use of pure *cis*- and *trans*-isomers did not increase the yield.

1,1,1,6,6,6-Hexanitrohex-3-yne (VII) was obtained in 72% yield by the double decomposition reaction between 1,4-dibromobut-2-yne and the silver salt of trinitromethane[9]:

$$BrCH_2{-}C{\equiv}C{-}CH_2Br + 2AgC(NO_2)_3 \rightarrow \underset{\text{(VII)}}{(NO_2)_3C{-}CH_2{-}C{\equiv}C{-}CH_2{-}C(NO_2)_3} + 2AgBr\ .$$

4-Trialkylsilyl(germyl)-1-nitrobut-1-ene-3-ynes are formed when products of the addition of nitrogen tetroxide and iodine to the corresponding vinylacetylene derivatives of the elements are dehydroiodinated by lead acetate[12-14]. The hydrolytic cleavage of the C–E bond (where E is an element) in butenyne derivatives of the elements leads to 1-nitrobut-1-en-3-yne[11] (VIII):

$$CH_2{=}CH{-}C{\equiv}C{-}Si\,(Ge)\,R_3 \xrightarrow{N_2O_4,I_2} NO_2CH_2{-}CHI{-}C{\equiv}C{-}Si\,(Ge)\,R_3 \rightarrow$$
$$\rightarrow NO_2CH{=}CH{-}C{\equiv}C{-}Si\,(Ge)\,R_3 \xrightarrow{8M\ HClO_4} \underset{\text{(VIII)}}{NO_2CH{=}CH{-}C{\equiv}CH}\ .$$

Acetylenic nitroglycols have been obtained by the condensation of acetylenic aldehydes with nitroalcohols[15,16]:

$$R{-}C{\equiv}C{-}\overset{\overset{O}{\parallel}}{C}{<}_{H} + NO_2CH_2{-}CH_2OH \rightarrow R{-}C{\equiv}C{-}CH(OH){-}CHNO_2{-}CH_2OH\ .$$

III. STRUCTURE AND PHYSICAL PROPERTIES

The study of the physical properties of α-nitroacetylenes led to definite conclusions concerning the conjugation of the highly electrophilic nitro-group with the C≡C bond.

α-Nitroacetylenes are pale yellowish-green liquids with a strong lachrymatory smell resembling that of lower nitro-olefins.

Table 1. Ultraviolet spectra of α-nitroalkylacetylenes and their ethylenic analogues[3].

No.	Compound	$\lambda_1(\pi{-}\pi^*)$ nm	lg ε_1	$\lambda_2(\pi{-}\pi^*)$ nm	lg ε_2	Solvent
1	t-Bu–C≡CNO_2	238	3.90	290	1.5	n-Hexane
2	i-Pr–C≡CNO_2	239	3.84	290	2.2	Cyclohexane
3	n-Pr–C≡CNO_2	235	3.88	290	2.7	n-Hexane
4	t-Bu–CH=$CHNO_2$ (*trans*)	228	4.02	310–320	2.8	n-Heptane
5	i-Pr–CH=$CHNO_2$ (*trans*)	227	3.70	—	—	n-Heptane
6	Me–CH=$CHNO_2$ (*trans*)	225	4.01	295–310	2.9	n-Heptane

The ultraviolet spectra of nitroacetylenes resemble those of *trans*-nitro-olefins. The short-wavelength ultraviolet band of nitroacetylenes undergoes a bathochromic shift relative to nitro-olefins and the extinction coefficient is reduced, which is characteristic of acetylenic systems in relation to their ethylenic analogues[22].

It has been suggested that the absorption at 290 nm (shoulder) is associated with a weak $\pi{-}\pi^*$ transition in the nitro-group of the $C{\equiv}CNO_2$ fragment[22,23].

The asymmetric stretching vibration band of the conjugated nitro-group in the spectra of α-ethylenic nitro-compounds is in the range 1517–1530 cm^{-1} and the band due to the symmetrical stretching vibrations is in the range ~ 1340–1350 cm^{-1}. The difference between the asymmetric and symmetric stretching vibration wavenumbers, which is an important characteristic of nitro-olefins, thus amounts to $\Delta\nu \simeq 180$ cm^{-1}. The substitution of a hydrogen atom at the β-carbon atom in nitroalkenes by a bromine atom leads to an increase of the asymmetric vibration wavenumber, a decrease of the symmetric vibration wavenumber, and an appreciable increase of the difference between them ($\Delta\nu = 218 \pm 7$ cm^{-1})[24,25].

Table 2. Characteristic wavenumbers in the infrared spectra of nitroacetylenes[3].

Compound	ν_{NO_2}, cm^{-1}		$\nu_{C\equiv C}$, cm^{-1}	ν_{C-N}, cm^{-1}
	asym.	sym.		
t-Bu–C≡CNO_2	1515	1330	2235 (s.) 2270 (w.)	730
i-Pr–C≡CNO_2	1510	1345	2245 (s.) 2210 (w.)	730
n-Pr–C≡CNO_2	1515	1348	2260 (s.) 2200 (w.)	730

Table 3.

Compound	$\nu_{C\equiv C}$, cm^{-1}		References
t-Bu–C≡CH	2105		28
t-Bu–C≡C–$CONH_2$	2245	2230	3
t-Bu–C≡C–COOEt	2260	2230	3
t-Bu–C≡C–CN	2325	2270	3
t-Bu–C≡C–NMe_2	2260	2230	3
t-Bu–C≡C–N(Ph)Me	2280	2245	3
t-Bu–C≡C–NO_2	2270	2235	3
t-Bu–C≡C–Cl	2243	2170	27
t-Bu–C≡C–Br	2216		27
t-Bu–C≡C–I	2191		27
$Me_3SiC{\equiv}C{-}NO_2$	2165		27
$Me_3SiC{\equiv}C{-}Cl$	2137		27
$Me_3SiC{\equiv}C{-}Br$	2126		27
$Me_3SiC{\equiv}C{-}I$	2100		27

The symmetric and asymmetric stretching vibration bands of the nitro-group in the infrared spectra of nitroacetylenes are very intense, the latter being displaced towards shorter wavelengths (1510–1515 cm^{-1}) compared with nitro-olefins and halogenonitro-olefins[3,24,25]; $\Delta\nu \simeq$ 165 cm^{-1}. The conjugation of the nitro-group with the multiple bond apparently has the greatest effect on the intensity of the symmetric stretching vibration band of the nitro-group: in the spectra of nitroacetylenes this band is much more intense than the band of the asymmetric vibrations, while in the spectra of nitro-olefins the intensities of these bands are approximately equal (in the spectra of aliphatic nitroalkanes the symmetrical stretching vibration bands of the nitro-group are of moderate intensity)[26].

The infrared spectra of α-nitroacetylenes show a splitting of the absorption band of the triple bond (Table 2), which is characteristic of disubstituted acetylenes (for

example, of trifluoropropyne and perfluorodimethylacetylene[3,27]; see also Table 3). The additional bands are accounted for by mechanical interactions; they are also regarded as overtones or combination bands. However, the reason for the splitting of the absorption band of the triple bond still remains controversial[22,27,28].

Comparison of the infrared spectra of halogenoacetylenes containing t-butyl and trimethylsilyl groups showed that in the latter case $\nu C{\equiv}C$ is reduced by 106–90 cm^{-1}.

In relation to t-butylnitroacetylene, the stretching vibration band of the C≡C bond in trimethylsilylnitroacetylene ($\nu C{\equiv}C$ = 2165 cm^{-1}) undergoes a steady bathochromic shift by about 10 cm^{-1} and its intensity falls, which may be a consequence of the π–d interaction in the $\rangle Si-C{\equiv}C$ group.

The 730 cm^{-1} band, which can be assigned to the C–N stretching vibrations, is constant in the spectra of all nitroacetylenes[3]. The information about the ^1H NMR spectra of nitroalkenes is extremely limited[29,30].

The ^1H NMR spectra of t-butyl-, isopropyl-, and n-propyl-nitroacetylenes proved to be very simple, as expected, and contained only signals corresponding to the protons of the alkyl groups.

Table 4.

Compound	δ, p.p.m.	Δδ, p.p.m.	References
t-Bu–CH=CH_2	1.00	—	31
t-Bu–CH=$CHNO_2$	1.15	0.15	3
t-Bu–C≡CH	1.20	—	31
t-Bu–C≡CNO_2	1.34	0.14	3
t-Bu–C≡C–COOEt	1.32	0.12	3
t-Bu–C≡C–CN	1.32	0.12	3

The shifts of the proton signals of the Me_3C group in the α-position relative to the multiple bond under the influence of various electrophilic substituents (all the compounds were used as solutions in CCl_4), which are listed in Table 4, illustrate the influence of the nitro-group.

IV. CHEMICAL PROPERTIES

α-Nitroacetylenes are extremely unstable. They change on storage or heating much faster than the lower nitroalkenes[32,33], 1-nitrobuta-1,3-diene[34], and also fluoroacetylenes[35].

Under the conditions of gas–liquid chromatography (t = 107–119°C), t-butylnitroacetylene (IV) did not change, isopropylnitroacetylene (V) decomposed to the extent of 30–50%, and n-propylnitroacetylene (VI) decomposed to the extent of 80–90%.

It was found by gas–liquid chromatography and infrared spectroscopy that the half-life at room temperature is 2–3 days for compound (IV), 10 h for unpurified specimens of compound (V), and 1–2 h for compound (VI).

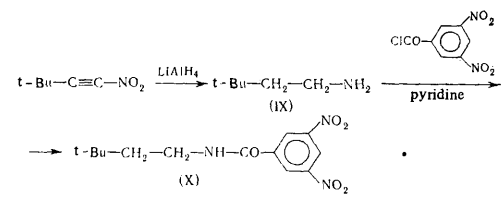
The thermal stability of compound (IV) has been studied in greatest detail. It has been shown that in 20% solution in toluene (IV) decomposes to the extent of 50% at 80–85°C in 30 min, the decomposition being almost complete after 10 h. Compound (IV) distills at 55°C/15 mmHg with partial decomposition. It melts at about –3°C.[3]

In dilute solutions in non-polar solvents (IV) is stable at 110–120°C. The type of transformation of nitroacetylenes on storage and heating has not been established.

The inductive effect of the nitro-group is very strong and comparable to the inductive effect of fluorine[36]. Therefore the oligomerisation of t-butylnitroacetylene and t-butylfluoroacetylene should presumably proceed similarly. Trifluoromethylacetylene is converted on storage into substituted benzene isomers and certain tetrameric products[37,38]. However, after standing for one month at room temperature, the products of the oligomerisation of compound (IV) contained, according to gas–liquid chromatographic data, more than 20 compounds in addition to the starting material, from which only one adduct (yield 1%) corresponding to the formula $C_{12}H_{18}N_4O_8$ (two molecules of t-butylnitroacetylene combined with an N_2O_4 molecule) could be isolated.

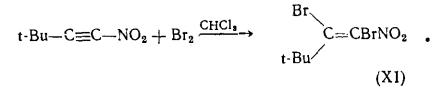
1. Hydrogenation

To demonstrate the structure of compound (IV), it was subjected to catalytic hydrogenation over platinum oxide, which yielded a mixture of the expected amine (IX) and, as shown by ^1H NMR, a dimeric compound corresponding to a symmetrically disubstituted hydrazine[3]. The reduction of compound (IV) by lithium tetrahydroaluminate in ether yielded the amine (IX), which was isolated in the form of the 3,5-dinitrobenzoyl derivative (X)[39]:



2. Bromination

The reaction of t-butylnitroacetylene with bromine in chloroform proceeds with slight evolution of heat and leads to 1,2-dibromo-1-nitroethylene in almost quantitative yield:



(XI)

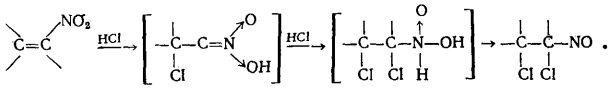
The ^1H NMR spectrum of this compound contains a singlet with δ = 1.5 p.p.m. corresponding to the protons of the t-butyl group, which is displaced to a lower field compared with the initial nitroacetylene[3].

The mechanism of this seemingly elementary reaction requires special consideration. The reaction of bromine with olefins and acetylenes is regarded as electrophilic addition[40]. However, the acceleration of the bromination of substituted tolanes (regardless of the nature of the substituents)[41] suggested that the first stage in these non-catalysed reactions involves the addition of the nucleophilic agent[42]. The situation in the case of nitro-olefins and nitroacetylenes is still more complicated owing to the possibility of acid catalysis[43] by the traces of HBr and HCl present in chloroform and responsible for the nucleophilic attack by bromine.

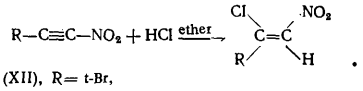
The lack of experimental data precludes the prediction of the stereochemical sequence of both the catalysed and non-catalysed additions to nitro-compounds containing multiple bonds.

3. Hydrochlorination

The interaction of nitro-olefins with anhydrous hydrogen chloride is known to involve a complex sequence of reactions[44] leading to nitro-olefins without an α-hydrogen atom, i.e. 1,2-dichloro-1-nitroisoalkanes[45]:

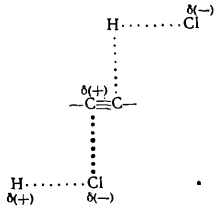


The hydrochlorination of nitroacetylenes (IV) and (V) even in the presence of an excess of HCl proceeds in a different way—with quantitative formation of *cis*-2-chloro-nitro-olefins[3]:



(XII), R= t-Bu,
(XIII), R= i-Pr.

Thus the 1,4-addition expected by analogy with nitro-olefins did not occur with nitroacetylenes. The mechanism of the addition of hydrogen chloride to nitro-acetylenes is probably different from that in the case of nitro-olefins. The *trans*-addition of hydrogen chloride to the triple bond is usually regarded as an electrophilic addition reaction, which is kinetically of third order (a reaction of the type AdE3). The transition state can be represented as follows[3]:



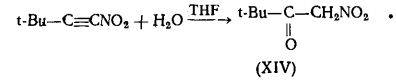
The addition of HCl to activated acetylenic systems, for example to acetylenedicarboxylates, is known to begin with nucleophilic attack[46-48] and to end with rapid protonation. Since nitroacetylenes should be still more electrophilic systems, in this case addition probably proceeds via the same mechanism.

4. Hydration

Water causes the polymerisation of lower nitro-olefins[44,49,50]. By selecting conditions eliminating polymerisation, it was possible to achieve the addition of water to the double bond with subsequent cleavage of the addition product into a carbonyl compound and a nitroalkane. Under alkaline conditions, this reaction is reversible, resulting in the formation of an aldol. The reaction is of the retroaldol type[51,52].

When nitroethylene was treated with a cold dilute sulphuric acid solution, the intermediate nitroalcohol was isolated[53].

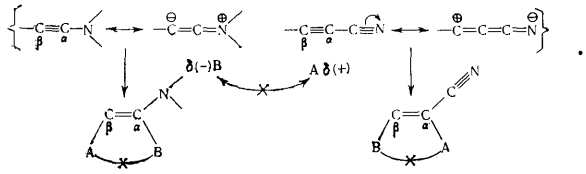
t-Butylnitroacetylene is hydrated much more readily than nitro-olefins and is smoothly converted under mild conditions (tetrahydrofuran, 20°C, 24 h) into 3,3-dimethyl-1-nitrobutan-2-one (XIV)[3]:



(XIV)

5. Nucleophilic Addition

By analogy with nitroalkenes, it was to be expected that nitroacetylenes would tend to undergo nucleophilic addition reactions. Substituted acetylenes conjugated with nucleophilic and electrophilic groups differ in the order in which nucleophiles add to them:



The similarity of the electrophilic properties of the nitro-group and fluorine can be extended also to the chemical behaviour of nitro- and fluoro-acetylenes[54]. The closeness of the electronegativities of the nitro-group and fluorine follows from a comparison of the chemical shifts in the ^{1}H NMR spectra of the M–X systems associated with the electronegativity of the substituent X (Table 5) and also from a study[37] in which the electronegativities of the organic functional groups were calculated from the chemical shifts and the coupling constants of 5-endo-substituted norbornenes.

Table 5. The chemical shifts of the protons in Me–X (solvent CCl_4).[3]

X	NO_2	F	Cl	$Me_2\overset{\oplus}{N}$	CN	H
δ p.p.m.	4.72	4.67	3.46	3.33*	2.32	0.13**

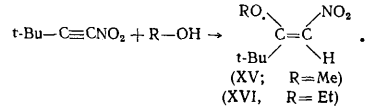
*In CF_3COOH.
**Gas.

The addition of alcohols and amines. α-Nitroacetylenes exhibit a marked electrophilic reactivity The reactions of t-butylnitroacetylene (IV), which is the most stable of the α-nitroacetylenes investigated, with nucleophilic agents proceed without catalysts at temperatures between −30° and 20°C. The electrophilic properties of the triple bond in this compound are much more pronounced than those of the triple bond in the heterosubstituted acetylenes of analogous structure[55] and the double bond in their ethylene analogues[56-58].

It has been shown that, under mild conditions (room temperature, 24 h, no catalyst) in methanol and ethanol, compound (IV) is smoothly converted into the corresponding *cis*-nitrovinyl ethers (yield 95%).

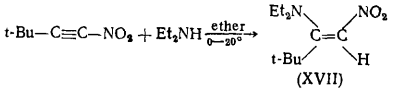
The enhanced intensity of the infrared bands of the double bond (1615, 1618 cm^{-1}) confirms the occurrence of

unhindered conjugation of the double bond with the nitro-group, which is possible only in the *cis*-form of the nitro-vinyl ether[3]:



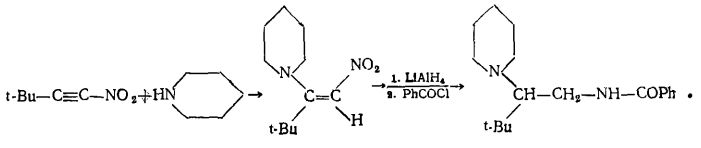
(XV; R=Me)
(XVI, R=Et)

It is known that ammonia and primary and secondary aliphatic amines readily add to nitro-olefins[49] and also cause their polymerisation[50]. The reaction of compound (IV) with aliphatic amines is exothermic and reaches completion with inflammation. However, the reaction with diethylamine in ethereal solution under controlled conditions gives rise to high yields of the expected adducts[3]:



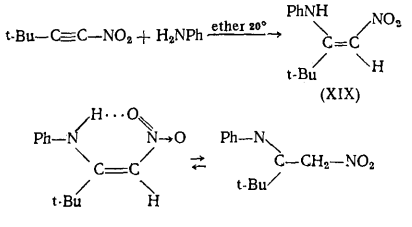
(XVII)

The product of the addition of piperidine to compound (IV) was not isolated in a pure form, but was identified as the benzoyl derivative of its hydrogenation product (XVIII):



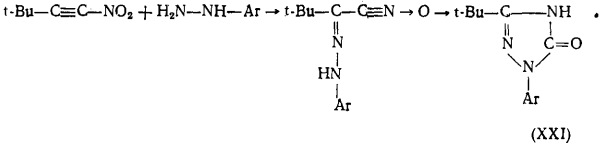
(XVIII)

The reaction with aniline is accompanied by the formation of the normal *trans*-addition product (XXa), which is in equilibrium with its tautomer (XXb)[3]:



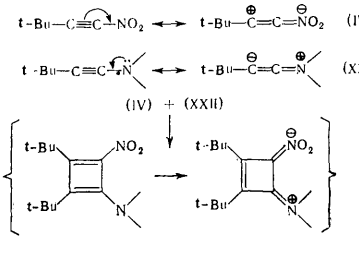
(XXa) (XXb)

Viehe and coworkers[59] showed recently that the reaction of compound (IV) with arylhydrazines results in the formation of 1,3-disubstituted 1,2,4-triazolin-5-ones (XXI):



(XXI)

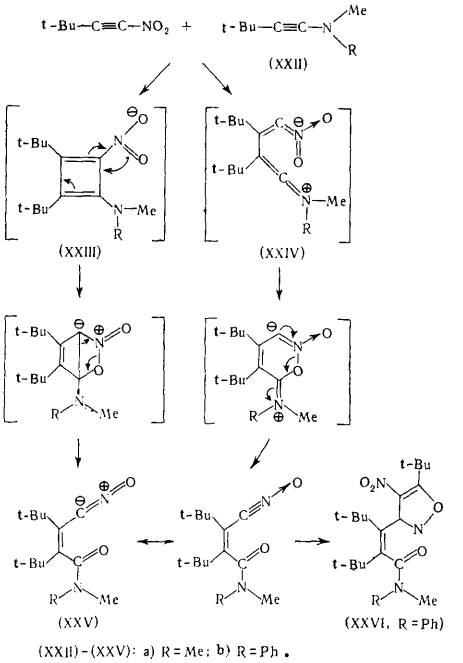
The high and opposed polarisations of t-butylnitro- and amino-acetylenes suggested the possibility of a direct combination of these compounds into the cyclobutadiene system via the mechanism:



The attempts at the synthesis of such systems on the basis of α-nitroenamines, undertaken by Breslow et al.,[60] were unsuccessful.

On the other hand, according to infrared spectroscopic data, the reaction of compound (IV) with (XXIIa) proceeds quantitatively with formation of compound (XXVa) (Scheme 1), which, however, could be isolated in only 29% yield. Compound (XXVc) was isolated similarly (in 21% yield); in this case there is in addition a competing reaction involving the 1,3-dipolar addition of compound (IV) to (XXVb), leading to the formation of an isoxazole derivative (XXVI)[3].

Scheme 1 (Ref.3)

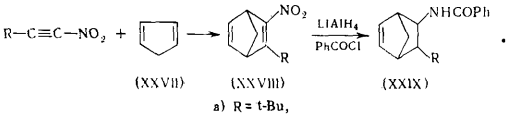


(XXII)-(XXV): a) R=Me; b) R=Ph.

6. Diels–Alder Reactions

The rate of Diels–Alder reactions is known to increase following the introduction of electron-donating substituents into the dienes and of electron-accepting substituents into the dienophiles (the "Alder rule")[61,62]. On this basis, it was possible to postulate that, when the t-butyl group in compound (IV) does not give rise to steric hindrance, the 1,4-cycloaddition of compound (IV) will be facilitated in the case of electron-rich alicyclic dienes.

However, among a large class of dienes [2,3-dimethylbuta-1,3-diene, cyclopentadiene(CPD), cyclohexa-1,3-diene, cyclohepta-1,3-diene, cyclo-octatetraene, tetracyclone, furan, 2,5-dimethylfuran, and diphenylisobenzofuran] only CPD (XXVII), one of the most reactive dienes[61,62], readily reacts with (IV) and also with (V) and (VI) to form the corresponding adducts (XXVIII). The rate of formation of adducts exceeds the rate of dimerisation of CPD.



(XXVII) (XXVIII) (XXIX)

a) R = t-Bu,
b) R = n-Pr,
c) R = i-Pr.

The adducts (XXVIII) and the CPD dimer were separated by column chromatography on silica gel. Compound (XXVIIIa) was obtained in high yield in the form of a yellow liquid, which was oxidised on standing in air. Similar compounds (XXVIII, b and c) proved to be even more sensitive to air. Despite the difficulty of its purification, the product (XXVIIIb) was identified by gas–liquid chromatography and ^{1}H NMR.[3]

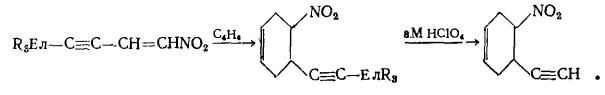
Compared with other dienophiles, nitro-olefins are known to be most reactive in relation to CPD[63,64]. However, in order to obtain information about the relative reactivity of the $-C\equiv C-NO_2$ system, it was necessary to compare, for example, compound (IV) with other acetylenic systems, the pronounced dienophilic properties of which are already known. Since the steric conditions must be the same, compounds (XXX) and (XXXI) were specially synthesised. It was shown[3] that the ratio of the rate constants for the reactions of CPD with (IV) and other members of the series

t-Bu—C≡C—NO_2 (IV); t-Bu—C≡C—COOEt (XXX); t-Bu—C≡C—CN (XXXI); t-Bu—CH=CHNO_2 (XXXII)

exceeds 10^4. The comparison of the reactivities of compound (IV) and the chloride of t-butylacetylenecarboxylic acid would probably be more instructive[3], since the determination of the rate constants for the Diels–Alder reaction of CPD (k) with *trans*-XCH≡CHX[65] and t-BuC≡CY indicates the similarity of the influence of the COCl and NO_2 substituents.

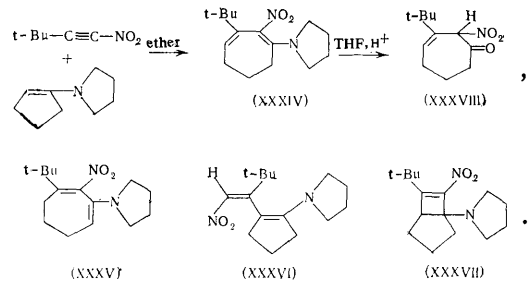
trans-X-CH=CHX					t-BuC≡CY	
Substituent X	COCl	COPh	CN	$COOMe_3$	NO_2	CN
k	6700	18	1,1	1.0	$>10^4$	1.0

4-Trialkylsilyl- and 4-trialkylgermyl-1-nitrobut-1-en-3-ynes (XXXIII) have also been used as dienophiles[11]. However, the condensation of these compounds with alka-1,3-dienes (buta-1,3-diene, CPD) involves only the olefinic group and the adducts formed are readily cleaved in an acid medium at the Si–C or Ge–C bond:



(XXXIII)

The reaction of compound (IV) with *N*-cyclopent-1-enylpyrrolidine is unusual[66]. By analogy with the reactions of enamines with nitro-olefins[67–76] and olefins containing other electrophilic substituents[67,68,77–80] and also with acetylenic systems[66,80–83], the formation of four products might have been expected in this case: a derivative of cycloheptadiene (XXXIV), its tautomer (XXXV), the Stork alkylation product (XXXVI), and a cyclobutene derivative (XXXVII):



However, the ^{1}H NMR spectrum of the resulting adduct showed the presence of the cycloheptadiene structure (XXXIV) alone. The structure of the adduct (XXXIV) was also confirmed by mild acid hydrolysis leading to the α-nitroketone (XXXVIII).

The addition of enamines to nitroacetylenes proceeds in a complex manner in a number of stages, which is confirmed by the difference between the infrared spectrum recorded immediately after the completion of the reaction and that of the product obtained after recrystallisation. An unstable product (XXXVII) is probably formed initially (the mode of addition is determined by the steric hindrance due to the *cis*-t-butyl group), and rearranges to compound (XXXIV) isolated finally. The reaction of nitroacetylenes with cyclic enamines constitutes a convenient synthetic method for the expansion of the ring by two carbon atoms[66].

The data quoted in this review demonstrate the absence of a complete analogy in the behaviour of ethylenic and acetylenic nitro-compounds. The study of nitroacetylenes has only just begun and presumably in the immediate future new interesting evidence will be obtained for the mutual influence of the atoms in compounds of this class and for the relation between their electronic structure and reactivity; also a wide variety of their synthetic possibilities will be discovered.

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Chemical Separation of Uranium Isotopes

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A brief survey is made of published work on various methods (electrochemical, chemical, extraction, and ion exchange) for separating the uranium isotopes 235 and 238. Attention is paid mainly to ion exchange using different states of oxidation of uranium in aqueous and organic solutions. The bibliography contains 70 references.

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I. INTRODUCTION

The separation of isotopes is based on differences in their physical and chemical properties. Since such differences are small, and diminish with increase in the atomic number of the element, the separation of isotopic mixtures is a very difficult task. Differences in the properties of isotopic varieties are obviously due to the difference in their masses.

Only physical methods—gas diffusion and centrifuging—have been developed for the industrial separation of uranium isotopes[1]. In several countries research has now been started with the aim of developing chemical methods for separating the isotopes of uranium.

II. BRIEF HISTORICAL SURVEY OF CHEMICAL METHODS FOR SEPARATING URANIUM ISOTOPES

During recent years several researches have been published in the foreign periodical press on chemical methods for separating uranium isotopes. Such methods can be classified as (i) electrochemical, (ii) chemical exchange in aqueous solution, (iii) extraction, and (iv) ion exchange. Work on the chemical separation of uranium isotopes was begun and continued during the Second World War by Brewer and Madorsky[2] using countercurrent electrical migration, which involved a difference in the kinetic properties of the ions. Their results were published towards the end of the 1940s.[3,4] In 1953 these workers reported briefly[5] that they had used ionic mobilities to enrich uranium with the light isotope from 0.72% to 2.8%.

A process for fractionating uranium isotopes, patented by Woodward[6] in 1957, was based on isotopic exchange between uranium(IV) and uranium(VI) ions in an acidic aqueous solution. In such solutions the quadrivalent ions become enriched with uranium-238, and the sexivalent ions with uranium-235. When two or more isotopes are present in solution, those of highest atomic weight tend to concentrate in the lower state of oxidation, and the others in the higher state. Woodward conducted isotopic exchange in aqueous hydrochloric acid containing 2% each of uranium(IV) and uranium(VI) (pH 1.5–1.9 for 1 h); after the exchange uranium(IV) was precipitated as the dioxalate, which after several intermediate operations was converted into the tetrachloride and used in the preceding stage of the process, while the filtrate was transformed into uranyl chloride, which was submitted to the following stage of

enrichment. This process of chemical enrichment is difficult to adapt to multistage working, since it involves many intermediate operations (precipitation, filtration, ignition).

Twitchell, Williams, and Clark[7] concentrated uranium-235 by chemical exchange combined with counterflow electrical migration: uranium(IV) and uranium(VI) moved in opposite directions on the latter principle, whose application had given good results in concentrating potassium, chlorine, and copper isotopes. It was shown that uranium(IV) could be transported from cathode to anode by the electrolyte flowing countercurrent to the uranium(VI) migrating to the cathode. After the cell had operated for 1400 h the uranium-235 content had increased from 0.7111% to 0.7171%. However, it was admitted[7] that this method involved many technical difficulties.

A 1958 patent[8] described a chemical method of isotopic fractionation of uranium based on extraction. This started from the suggestion[9] that the achievement of efficient separation entailed that the chemical state of an isotope in the organic phase should differ from its chemical state in the aqueous phase. This requirement was satisfied by a system in which a metal ion in the aqueous phase was in equilibrium with a chelate or other complex of the metal in an organic solvent immiscible with the aqueous solution. It was established that isotopic exchange took place when an acidic aqueous solution of uranium(IV) was in contact with a water-immiscible organic solvent in which was dissolved a water-insoluble chelate complex of uranium(IV), as a result of which uranium-235 was concentrated in the aqueous solution, and uranium-238 was distributed as the chelate complex into the organic solvent. Cupferron was recommended to form a chelate complex of uranium(IV): uranium cupferronate is insoluble in water, but soluble in many organic solvents. The most effective solvent was chloroform, which ensured rapid phase separation. Since isotopic fractionation requires many stages, countercurrent contact between organic and aqueous phases, as is usual in continuous countercurrent extraction, was tested and proposed. During the isotopic fractionation the uranium transferable by the organic phases passes successively from stage to stage in one direction, while the uranium-containing aqueous solution passes in the opposite direction. An aqueous solution enriched with uranium-235 was withdrawn at one end of the apparatus, and an organic solution enriched with uranium-238 at the opposite end.

It was proposed also to accomplish isotopic fractionation by countercurrent contact between solutions passing through a vertical packed column. A glass helix-filled 9-m column of diameter 1 cm was used, the aqueous solution flowed upwards, and the organic solution downwards. Clewett et al.[8] considered that the exchange reaction

$$^{238}UCl_{4\,aq} + {}^{235}U[C_6H_5N(NO)O]_4 \rightleftarrows {}^{235}UCl_{4\,aq} + {}^{238}U[C_6H_5N(NO)O]_4 \quad (1)$$

accomplished in this way might lead to a single-stage separation factor of 1.002.

A brief communication by Spedding and Powell[10] also indicated the possibility of achieving this separation factor. Uranium isotopes were separated in a uranyl solution together with a cation-exchange resin. The uranium band was eluted through a column filled with the copper form of Dowex 50 × 8 sulphonated cation-exchange resin (50–100 mesh) by means of 0.005 M aqueous diammonium magnesium ethylenediaminetetra-acetate. The isotopic exchange is described by the equation

$$^{238}UO^{2+}_{2\,aq} + {}^{235}UO_2R \rightleftarrows {}^{238}UO_2R + {}^{235}UO^{2+}_{2\,aq}, \quad (2)$$

where UO_2R and UO_2^{2+} denote uranyl ions in the exchanger and in the aqueous solution respectively. With a band 28 cm long traversing a distance of 90 cm isotopic changes of 4–5% were reported[10] at both ends of the band, enrichment with uranium-235 being observed in the leading portion of the band.

The results obtained by the above workers on the extraction and ion-exchange separation of uranium isotopes led them to make extremely optimistic forecasts of large-scale enrichment. However, it was reported later[11] that attempts to use the extraction method for separating uranium isotopes had been unsuccessful, since cupferron oxidised rapidly, and the resulting oxidation products prevented normal functioning of the countercurrent column.

Finally in 1969 Rutenberg and Drury[12] refuted the above results. They used new equipment to make accurate measurements of isotopic changes in the system formed by a chloroform solution of uranium cupferronate and an aqueous hydrochloric-acid solution in the uranium band of the above experiment by Spedding and Powell. The single-stage separation factor was found to be far lower than the published value (1.002) in both extraction and ion-exchange systems, respectively 1.00007 ± 0.00001 and 1.00006 ± 0.00005. Calculations showed that the above processes for separating uranium isotopes were unacceptable both technically and economically.

The separation of uranium isotopes by chemical methods has been widely investigated in Japan, where attention has been concentrated on the use of ion-exchange resins. A joint paper on this problem was presented by Kakihana et al.[13] at the Third International Conference on the Peaceful Uses of Atomic Energy held in Geneva in 1964. A brief account was given of the theory of the separation of uranium isotopes by isotopic exchange, together with experimental results for an exchanger in a solution of uranium in aqueous hydrochloric acid.

In March 1970 the Japanese newspaper *Asahi Shimbun*[14] published a report on the Annual Symposium of Japanese Nuclear Scientists containing experimental results on the enrichment of uranium by chemical methods. An ion-exchange column of height 1 m and cross-section 1 cm^2 was used with Amberlite IRA-120B, a sulphonated cation-exchange resin. A single passage of an acid sulphate solution of uranium increased the uranium-235 content by 1.017%; fractions of the enriched uranium solution were withdrawn first from the column. On the basis of these results it is planned to set up a new experimental plant 10–30 times as powerful. Several advantages of the new process are emphasised: (*a*) the technical equipment is considerably simpler; (*b*) use of the aggressive and toxic uranium hexafluoride is avoided; and (*c*) Japanese experts estimate that the capital cost of constructing an industrial plant to produce 1000 tonnes of 3% uranium-235 annually will be less than 10% of the cost of constructing a gas-diffusion plant.

A news item[15] referred to Japanese reports of similar work in France.

III. SEPARATION OF URANIUM ISOTOPES BY ION EXCHANGE

The first experiments on the separation of stable isotopes by ion exchange were made more than thirty years ago by Taylor and Urey[16,17]. Since then many investigations have been made on the separation of lithium, boron, sodium, calcium, and nitrogen isotopes on a sulphonated cation-exchange resin in an aqueous electrolyte

solution. However, low separation factors were obtained except in work[18] on the ion-exchange separation of the isotopes of nitrogen. Experiments on uranium isotopes[19] gave separation factors <1.001. Kakihana et al.[20] explained such results by the almost identical states of the isotopes in the external aqueous solution and in the sulphonated cation-exchange resin: systems in which the isotopes are in different chemical states in the phases must be chosen to obtain higher values.

Japanese work on the chemical separation of uranium isotopes has been based on Kakihana and Kurisu's theory of separation by isotopic exchange between uranium(IV) and uranium(VI). These workers made detailed theoretical investigations on the factors on which the efficiency of separation of the isotopes depends[21,22], and deduced the main equation for the separation factors.

Theoretical and experimental investigations published hitherto are surveyed below.

1. ISOTOPIC EXCHANGE IN VARIOUS CHEMICAL SYSTEMS

(*a*) General Principles

Isotopic exchange can be effected by the transfer of isotopic atoms and of electrons. An example of the former is exchange in complex compounds. The first studies on this problem were made by Grinberg and Filinov[23,24]. Numerous subsequent investigations have established that the rate of isotopic exchange in complexes is greatly influenced by such factors as the nature of the ligand[25,26], the sign of the ionic charges[27], the coordination number[28,29], etc.

Isotopic exchange by the transfer of electrons takes place in redox systems. Reactions of this type involve essentially not the exchange of isotopes but a change in their valency states. For example, the exchange of iron between $FeCl_2$ and $*FeCl_3$

$$Fe^{3+} + {}^{*}Fe^{3+} \rightleftarrows Fe^{3+} + {}^{*}Fe^{2+} \qquad (3)$$

can be regarded as the result of two processes leading to electron transfer from Fe^{2+} to $*Fe^{3+}$:

$$Fe^{3+} \rightleftarrows Fe^{3+} + \bar{e} \quad \text{(conversion of unlabelled } Fe^{II} \text{ into } Fe^{III}) \qquad (4)$$

$$*Fe^{3+} + \bar{e} \rightleftarrows {}^{*}Fe^{2+} \quad \text{(conversion of labelled } Fe^{III} \text{ into } Fe^{II}) \ . \qquad (5)$$

In reality the two stages are not separate, and the electron passes directly from one ion to the other[30]. Such exchange reactions, observed in reversible redox systems, occur at different rates. The rate of exchange is strongly dependent on concentration, acidity, additions of foreign ions, etc.[30]

Investigations on isotopic exchange between uranium(IV) and uranium(VI) in various systems is of great value in connection with the problem of separating uranium isotopes by chemical methods.

(*b*) Hydrochloric-acid Solutions

Detailed investigations of the kinetics and the mechanism of isotopic exchange between uranium(IV) and uranium(VI) were made by Rona[31], who studied the reaction

$$U^{IV} + {}^{*}U^{VI} \rightleftarrows {}^{*}U^{IV} + U^{VI} \ , \qquad (6)$$

where the asterisk denotes the radioactive uranium-233 isotope. The experiments showed that the order of the rate of exchange with respect to the hydrogen-ion concentration was ~3. Rona showed also that the rate of exchange was independent of the addition of neutral salts, the concentration of chloride ions, and illumination. According to Woodward[6], however, light accelerates the reaction considerably (both workers used the light from a tungsten lamp).

In order to understand the mechanism of the above exchange reactions it is important to know the ionic forms of uranium(IV) and uranium(VI). There is weighty evidence that uranium(VI) is present as UO_2^{2+} in moderate acid concentrations[32]. Quadrivalent uranium is assumed to exist as the equilibrium mixture

$$U^{4+} \rightleftarrows U(OH)^{3+} \rightleftarrows U(OH)_2^{2+} \rightleftarrows U(OH)_3^{+} \ . \qquad (7)$$

Rona suggests[31] that, in the uranium(IV–VI) exchange system, the last form $U(OH)_3^+$ will react readily with the uranyl ion to form a complex containing an oxygen bridge between the two ions:

$$U(OH)_3^+ + UO_2^{2+} \underset{\longleftarrow}{\overset{2H_2O}{\rightleftarrows}} Z^{3+} + 2H^+ \ , \qquad (8)$$

where Z^{3+} is a hypothetical intermediate ion, which may have the structure

$$\left[\begin{array}{c} O{=}U{-}O{-}U{-}OH \\ \quad | \quad\quad | \\ \quad OH \quad\ OH \end{array}\right]^{3+} \ .$$

This leads to the possible reaction mechanism of isotopic exchange

$$^{235}U(OH)_3^+ + {}^{238}UO_2^{2+} \rightleftarrows {}^{235}UO_2^{2+} + {}^{238}U(OH)_3^+ \qquad (9)$$

in which Z^{3+} is the intermediate activated complex taking part in the electron transfer

$$\left[\begin{array}{c} HO{-}{}^{235}U^{IV}{-}OH \\ \quad | \\ \quad OH \end{array}\right]^{+} + \left[\begin{array}{c} {}^{238}U^{VI}{=}O \\ \quad \| \\ \quad O \end{array}\right]^{2+} \rightleftarrows \left[\begin{array}{c} O{=}{}^{235}U{-}O{-}{}^{238}U{-}OH \\ \quad\quad | \quad\quad\quad | \\ \quad\quad OH \quad\quad OH \end{array}\right]^{3+} \rightleftarrows$$

$$\rightleftarrows \left[\begin{array}{c} {}^{235}U^{VI}{=}O \\ \quad \| \\ \quad O \end{array}\right]^{2+} + \left[\begin{array}{c} HO{-}{}^{238}U^{IV}{-}OH \\ \quad\quad | \\ \quad\quad OH \end{array}\right]^{+} \ . \qquad (10)$$

This isotopic exchange appears to be an exchange of ligands between uranium(IV) and uranium(VI) ions.

The effect of the concentration of hydrochloric acid on the rate of exchange was studied also by Kakihana et al.[33,34], who investigated the homogeneous exchange between natural uranium(IV) and impoverished uranium(VI) in various acid concentrations at 30, 50, and 70°C.

(*c*) Sulphuric-acid Solutions

Studies of the exchange between uranium(IV) and uranium(VI) in aqueous sulphuric acid were described by Betts[35] in 1948. This exchange occurs essentially between the sulphate complexes, in whose inner sphere sulphate ions are assumed to be accompanied by water molecules. The presence of the latter in the inner sphere, and especially of hydroxide ions, both in hydrochloric-acid and in sulphuric-acid solutions as assumed by Grinberg and Bykhovskii[36], facilitates the transition from U^{4+} to UO_2^{2+}.

Baechmann and Lieser[37] found that, in solutions containing sulphate ions in the dark, the rate of electron exchange between uranium(IV) and uranium(VI) is proportional to their concentrations and inversely proportional to the cube of the hydrogen-ion concentration. The reaction velocity is governed by the stage of disproportionation

of uranium(V), present in small quantities in equilibrium with uranium(IV) and uranium(VI). This conclusion was based on Betts' finding[35] that the rate of electron transfer between the latter valency states in sulphate solutions was far greater, and on Heal and Thomas's discovery[38] of higher uranium(V) concentrations, under illumination. The mechanism of electron transfer is represented by

$$U^{4+} + {}^{*}U^{6+} \rightleftarrows U^{5+} + {}^{*}U^{5+} \quad . \tag{11}$$

Subsequent disproportionation of U^{5+} yields $*U^{4+}$:

$$U^{5+} + {}^{*}U^{5+} \rightleftarrows U^{6+} + {}^{*}U^{4+} \quad . \tag{12}$$

Electron exchange between uranium(IV) and uranium(VI) has been investigated also in several other solutions—oxalate[36], perchlorate[39], and aqueous organic[40-43].

(*d*) Cation-exchange Resin in Hydrochloric-acid Solution

Isotopic exchange in a system comprising a cation-exchange resin in a hydrochloric-acid solution was studied by Shimokawa and Nishio[44]. Granules of Dowex 50 × 4 containing ions of impoverished uranium(IV) were placed in a solution of natural uranium(VI). At the start of the reaction a certain quantity of uranium(VI) ions passed into the resin from the solution, but all the uranium(IV) ions remained in the resin throughout the reaction with aqueous acid concentrations up to 1 *N*. Change in the relative content of the uranium(IV) isotope in the resin was followed mass-spectrometrically. Analysis of the system revealed two possible modes of exchange (on the basis that the reaction was bimolecular[45-47]).

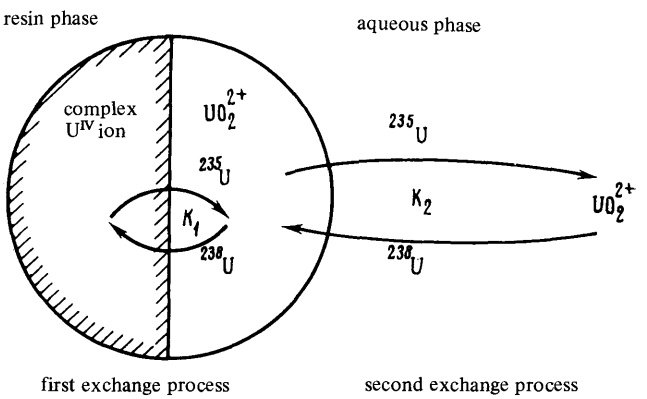


Figure 1. Diagram of two exchange processes.

1. First exchange process. With isotopic exchange between uranium(IV) and uranium(VI) occurring in the resin phase

$$^{235}U^{IV}_{res} + {}^{238}U^{VI}_{res} \overset{K_1}{\rightleftarrows} {}^{238}U^{IV}_{res} + {}^{235}U^{VI}_{res} \tag{13}$$

the isotopic exchange equilibrium constant $K_1 = 1.0007$ (i.e. $1/K_1 = 0.9993$). The fact that K_1 exceeds unity implies that sexivalent uranium is enriched with the 235 isotope when chemical equilibrium is established, and the quadrivalent state with uranium-238.

2. Second exchange process. Isotopic exchange between sexivalent uranium in the resin and sexivalent uranium in solution

$$^{235}U^{VI}_{res} + {}^{238}U^{VI}_{soln} \overset{K_2}{\rightleftarrows} {}^{238}U^{VI}_{res} + {}^{235}U^{VI}_{soln} \tag{14}$$

gives an equilibrium constant $K_2 = 1$. Reaction (13) is more rapid than reaction (14).

Thus isotopic exchange in a system comprising a solution and a cation-exchange resin is represented by the scheme

$$^{235}U^{IV}_{res} + {}^{238}U^{VI}_{soln} \overset{K}{\rightleftarrows} {}^{238}U^{IV}_{res} + {}^{235}U^{VI}_{soln} \quad , \tag{15}$$

whence the equilibrium constant $K = K_1K_2 = 1 + \epsilon$ or

$$K = \frac{^{238}U^{IV}_{res}}{^{235}U^{IV}_{res}} : \frac{^{238}U^{VI}_{soln}}{^{235}U^{VI}_{soln}} . \tag{16}$$

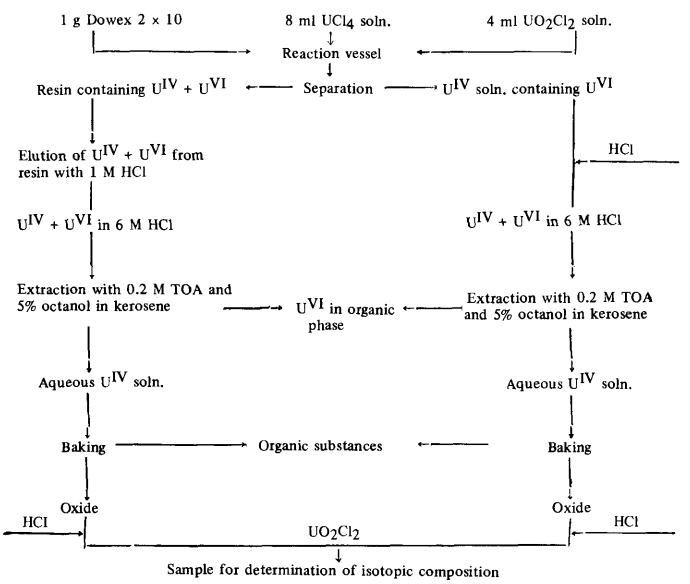
Fig. 1 illustrates diagrammatically the two exchange processes. It follows from Eqn. (15) that uranium-235 is concentrated in the uranium(VI) solution. The rate constant of isotopic exchange was greater in the resin phase than in solution by $\sim 10^3$–10^4, which indicates that the cation-exchange resin catalyses the isotopic exchange of uranium(IV) and uranium(VI).

(*e*) Anion-exchange Resin in Hydrochloric-acid Solution

The first results for the isotopic exchange of uranium(IV) and uranium(VI) in an anion-exchange resin in aqueous hydrochloric acid were presented at the Third International Conference on the Peaceful Uses of Atomic Energy[13]. The experimental procedure (Scheme 1) involved treating samples of Dowex 2 × 8 with 8 M hydrochloric acid containing natural uranium(IV) and impoverished uranium(VI); after ion-exchange equilibrium had been established, the change in the relative content of uranium-235 was monitored at intervals, both for uranium(IV) in the resin and for uranium(VI) in the solution.

Scheme 1.

Study of electron exchange between uranium(IV) and uranium(VI) in a hydrochloric-acid solution impregnating an anion-exchange resin.



The experimental results showed that quadrivalent uranium is enriched with the 235 isotope, and sexivalent uranium with the 238 isotope. Isotopic exchange can occur in three possible ways:

$$^{238}\overline{U}^{IV} + {}^{235}\overline{U}^{VI} \overset{k_1}{\rightleftarrows} {}^{238}\overline{U}^{VI} + {}^{235}\overline{U}^{IV} \quad , \tag{17}$$

$$^{238}U^{IV} + {}^{235}\overline{U}^{IV} \overset{k_2}{\rightleftarrows} {}^{235}U^{IV} + {}^{238}\overline{U}^{IV} \quad , \tag{18}$$

$$^{235}\overline{U}^{VI} + {}^{238}U^{IV} \overset{k_3}{\rightleftarrows} {}^{235}U^{IV} + {}^{238}\overline{U}^{VI} \quad , \tag{19}$$

$$\frac{d[^{235}\overline{U}^{IV}]}{dt} = k_1\{[^{235}\overline{U}^{VI}][^{238}\overline{U}^{IV}] - [^{235}\overline{U}^{IV}][^{238}\overline{U}^{VI}]\} + k_2\{[^{238}U^{IV}][^{238}\overline{U}^{IV}] - [^{235}\overline{U}^{IV}][^{238}U^{IV}]\} \quad , \tag{20}$$

$$\frac{d[^{235}U^{IV}]}{dt} = k_2\{[^{235}\overline{U}^{IV}][^{238}U^{IV}] - [^{235}U^{IV}][^{238}\overline{U}^{IV}]\} + k_3\{[^{235}\overline{U}^{VI}][^{238}U^{IV}] - [^{235}\overline{U}^{VI}][^{235}U^{IV}]\} \quad , \tag{21}$$

$$\frac{d[^{235}\overline{X}^{VI}]}{dt} = k_1\{[^{235}\overline{U}^{IV}][^{238}\overline{U}^{VI}] - [^{235}\overline{U}^{VI}][^{238}\overline{U}^{IV}]\} + k_3\{[^{235}U^{IV}][^{238}\overline{U}^{VI}] - [^{235}\overline{U}^{VI}][^{238}U^{IV}]\} \quad , \tag{22}$$

where [U] and $[\overline{U}]$ represent uranium concentrations in solution and in the resin phase respectively. For simplicity we introduce the notation

$$[^{235}U^{IV}] + [^{238}U^{IV}] = a \qquad [^{235}U^{IV}] = af^{IV}$$
$$[^{235}\overline{U}^{IV}] + [^{238}\overline{U}^{IV}] = \overline{a} \qquad [^{235}\overline{U}^{IV}] = \overline{a}\overline{f}^{IV}$$
$$[^{235}\overline{U}^{VI}] + [^{238}\overline{U}^{VI}] = \overline{b} \qquad [^{235}\overline{U}^{VI}] = \overline{b}\overline{f}^{VI}$$

for the uranium concentrations and the isotopic fractions. During exchange a, $\overline{a}$, and $\overline{b}$ remain constant, while f^{IV}, $\overline{f}^{IV}$, and $\overline{f}^{VI}$ change. Formulae (20)–(22) become

$$\frac{1}{a\overline{b}} \cdot \frac{d\overline{f}^{IV}}{dt} = \frac{1}{a}\{\overline{f}^{VI} - \overline{f}^{IV}\}k_1 + \frac{1}{\overline{b}}\{f^{IV} - \overline{f}^{IV}\}k_2 \quad , \tag{20'}$$

$$\frac{1}{\overline{a}\overline{b}} \cdot \frac{df^{IV}}{dt} = \frac{1}{\overline{a}}\{\overline{f}^{VI} - f^{IV}\}k_3 + \frac{1}{\overline{b}}\{\overline{f}^{IV} - f^{IV}\}k_2 \quad , \tag{21'}$$

$$\frac{1}{a\overline{a}} \cdot \frac{d\overline{f}^{VI}}{dt} = \frac{1}{a}\{\overline{f}^{IV} - \overline{f}^{VI}\}k_1 + \frac{1}{\overline{a}}\{f^{IV} - \overline{f}^{VI}\}k_3 \quad . \tag{22'}$$

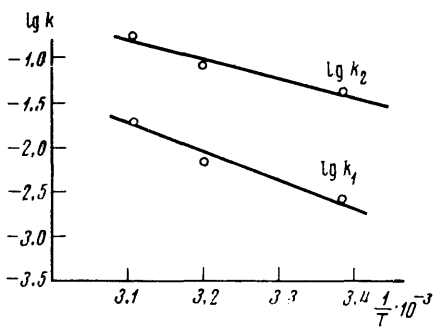


Figure 2. Temperature dependence of reaction rate constant.

The rate constants k_1, k_2, and k_3 can be calculated from Eqns. (20)–(22) by analysing the isotopic composition of samples f^{IV}, $\overline{f}^{IV}$, and $\overline{f}^{VI}$. The apparent reaction rate constant at 30°C was found to be $k_1 = 7.5 \times 10^{-4}$ M^{-1} min^{-1}, which was small in comparison with the value of 3500 [$?3.5 \times 10^{-3}$] M^{-1} min^{-1} in 8 M hydrochloric acid at this temperature. A possible explanation is that the resin phase contains less hydrochloric acid to accelerate this electron exchange[34] than does the acid solution, and that the exchangeable ions do not diffuse so easily in the resin as in the aqueous acid, owing to the effect of functional groups in the anion exchanger.

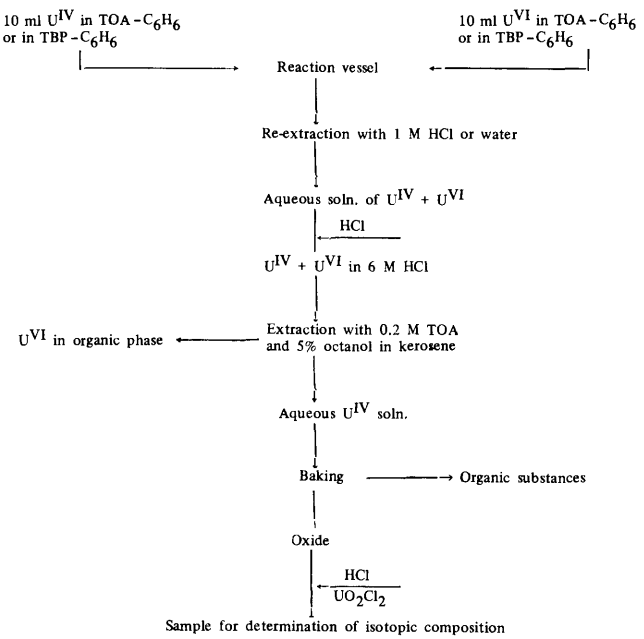
The temperature dependence of the logarithm of the rate constant is plotted in Fig. 2. The activation energy of the electron exchange between uranium(IV) and uranium(VI) in the anion-exchange resin was 22.9 kcal $mole^{-1}$. The closeness of this value to 24–25 kcal $mole^{-1}$ indicates similarity between the activated complexes of this electron exchange in the resin and in 6–10 M hydrochloric acid.

(*f*) Benzene Solution of Trioctylamine (TOA) and Tributyl Phosphate (TBP)

According to Gonda et al. benzene solutions of trioctylamine and tributyl phosphate are extremely promising media for electron exchange between uranium(IV) and uranium(VI).[48] The experimental procedure (Scheme 2) involves mixing equal volumes of benzene solutions of trioctylamine containing respectively natural uranium(IV) and impoverished uranium(VI); a similar operation was made with benzene solutions of tributyl phosphate. In both cases uranium(IV) is enriched with the heavier isotope, and uranium(VI) with the lighter isotope.

Scheme 2.

Study of U^{IV}–U^{VI} electron exchange in TOA–C_6H_6 and TBP–C_6H_6 systems.



The extent of exchange F was determined by means of the equation

$$F = \{f^{IV} - f_0^{IV}\} \cdot \{f_\infty^{IV} - f_0^{IV}\}^{-1} \quad , \tag{23}$$

where f_0^{IV}, f^{IV}, and f_∞^{IV} are the contents of the 235 isotope in uranium(IV) initially, after time t, and finally. The relation between F, the rate of exchange R, and the rate constant k is

$$\ln(1-F) = \ln\{f^{IV} - f_\infty^{IV}\} \cdot \{f_0^{IV} - f_\infty^{IV}\}^{-1} = -R\{[U^{IV}] + [U^{VI}]\} \cdot \{[U^{VI}] \cdot [U^{IV}]\}^{-1}t = -k\{[U^{IV}] + [U^{VI}]\}^{-1}t \quad . \tag{24}$$

The dependence of $\ln(1-F)$ on time is represented by a straight line, from whose slope we can determine R and k.

Rate of exchange increases with decrease in the concentration of trioctylamine or tributyl phosphate in benzene. The explanation is that the complexes of these solutes that are capable of exchange diffuse more easily into dilute than into concentrated solutions. In particular, true rate constants can be determined by measuring exchange in dilute solutions of trioctylamine and tributyl phosphate. The mechanism of exchange when the complex ions are extracted into a benzene solution of trioctylamine is similar to that in an anion-exchange resin.

2. SEPARATION OF URANIUM ISOTOPES IN AN EXCHANGER–SOLUTION SYSTEM CONTAINING URANIUM(IV) AND URANIUM(VI)

(*a*) Separation Factor of Uranium Isotopes

Since isotopic effects in chemical systems met in practice usually balance out, it proved impossible for a long time to obtain for uranium isotopes any appreciable separation factors defining the efficiency of particular systems. Experimental studies made in Japan with the aim of obtaining high separation factors for these isotopes were based on theoretical investigations by Kakihana and Kurisu[21,22,49,50], Ishida[51,52], and Shimokawa[44,53].

The separation factor for uranium isotopes can in general be expressed by the formula

$$^{235}_{238}S=\frac{[^{235}\overline{U}]}{[^{238}\overline{U}]}\cdot\frac{[^{238}U]}{[^{235}U]}=\frac{\Sigma[^{238}U^{IV}]+\Sigma[^{238}U^{VI}]}{\Sigma[^{235}U^{IV}]+\Sigma[^{235}U^{VI}]}\cdot\frac{\Sigma[^{235}\overline{U}^{IV}]+\Sigma[^{235}\overline{U}^{VI}]}{\Sigma[^{238}\overline{U}^{IV}]+\Sigma[^{238}\overline{U}^{VI}]}, \quad (25)$$

where $^{238}U/^{235}U$ is the molar ratio of the isotopes in solution, and $^{235}\overline{U}/^{238}\overline{U}$ the corresponding ratio in the ion exchanger. For a system containing only U^{4+} ions the separation factor is

$$S_1=\frac{\Sigma[^{238}U^{IV}]}{\Sigma[^{235}U^{IV}]}\cdot\frac{\Sigma[^{235}\overline{U}^{IV}]}{\Sigma[^{238}\overline{U}^{IV}]}\ . \quad (26)$$

When only uranyl ions UO_2^{2+} are present, we have

$$S_2=\frac{\Sigma[^{238}U^{VI}]}{\Sigma[^{235}U^{VI}]}\cdot\frac{\Sigma[^{235}\overline{U}^{VI}]}{\Sigma[^{238}\overline{U}^{VI}]}\ . \quad (27)$$

The electron exchange in solution can be written

$$^{235}U^{VI}+{}^{238}U^{IV}\rightleftarrows{}^{238}U^{VI}+{}^{235}U^{IV} \quad (28)$$

and that in the ion-exchange resin is represented by

$$^{235}\overline{U}^{VI}+{}^{238}\overline{U}^{IV}\rightleftarrows{}^{238}\overline{U}^{VI}+{}^{235}\overline{U}^{IV}\ . \quad (29)$$

The equilibrium constants of these electron exchanges are—for the solution

$$K_e=\frac{\Sigma[^{238}U^{VI}]}{\Sigma[^{235}U^{VI}]}\cdot\frac{\Sigma[^{235}U^{IV}]}{\Sigma[^{238}U^{IV}]} \quad (30)$$

and for the ion exchanger

$$\overline{K}_e=\frac{\Sigma[^{238}\overline{U}^{VI}]}{\Sigma[^{235}\overline{U}^{VI}]}\cdot\frac{\Sigma[^{235}\overline{U}^{IV}]}{\Sigma[^{238}\overline{U}^{IV}]}\ . \quad (31)$$

From (26), (27), (30), and (31) we obtain

$$\overline{K}_e=K_e\frac{S_1}{S_2}\ . \quad (32)$$

Mathematical rearrangement yields

$$^{235}_{238}S=S_2\left(\frac{S_1K_eS_2^{-1}+\bar{\rho}}{1+\bar{\rho}}\right)\left(\frac{K_e^{-1}+\rho}{1+\rho}\right)\ , \quad (33)$$

where $\rho=\Sigma[U^{VI}]/\Sigma[U^{IV}]$ and $\bar{p}=\Sigma[\overline{U}^{VI}]/\Sigma[\overline{U}^{IV}]$ are the molar ratios of uranium(VI) and uranium(IV) in the solution and in the ion exchanger respectively. Taking logarithms and rearranging slightly, we convert (33) into

$$\ln^{235}_{238}S=\ln S_2+\ln\left(1+\frac{S_1K_eS_2^{-1}-1}{1+\bar{\rho}}\right)+\ln\left(1+\frac{K_e^{-1}-1}{1+\rho}\right)\ , \quad (34)$$

which is the fundamental equation for the separation of uranium isotopes in a mixture of uranium(IV) and uranium(VI).

In view of Eqn. (32) we can write (34) in the form

$$\ln^{235}_{238}S=\ln S_2+\ln\left(1+\frac{\overline{K}_e-1}{1+\bar{\rho}}\right)+\ln\left(1+\frac{K_e^{-1}-1}{1+\rho}\right)\ , \quad (35)$$

which emphasises the important fact that the greater the difference between ρ and $\bar{\rho}$ the greater the contribution made by K_e to the separation factor. Uranium(IV) is adsorbed preferentially by a cation-exchange resin, and uranium(VI) by an anion-exchange resin. Consequently either resin may be a good secondary phase giving a high separation factor provided that electron exchange (which takes place very slowly in an ordinary aqueous solution) is accelerated by some catalyst, in particular by the resin itself.

(*b*) Separation of Uranium Isotopes by Means of a Cation-exchange Resin

Kakihana et al.[20,54] used frontal analysis to determine separation factors for a sulphonated cation-exchange resin in a hydrochloric-acid solution containing uranium(IV) and uranium(VI). Acid (0.6 M and 2 M) solutions of uranium were passed at 30 ml h^{-1} through a column (of height 100 cm and diameter 1 cm) filled with Dowex 50 × 12 in the hydrogen form (100–200 mesh). Since the experiments were made under non-equilibrium conditions, the separation factor was calculated by means of the approximate formula

$$^{235}_{238}S=1+\frac{D}{Q}\cdot\frac{1}{R_0} \quad (36)$$

in which

$$D=\Sigma d=\Sigma\Delta m\cdot\Delta R \quad (37)$$

is the total change in the uranium-235 content of the exchanger, Δm being the absolute uranium content of the sample, $\Delta R=R_0-R$, where R_0 and R are the uranium-235 contents in the initial solution and in the samples of eluate, and Q is the total quantity of uranium sorbed by the exchanger. The greatest impoverishment with respect to uranium-235 was observed in the early samples containing uranium(IV), and slight impoverishment in samples containing uranyl ions. The reason is that the light isotope is more strongly retained than uranium-238 in the cation-exchange resin. The single-stage separation factor in these experiments was 1.00028–1.00048.

In July 1968 some Japanese workers patented a counter-current method for enriching uranium isotopes by ion exchange, in which electron exchange was effected between uranium(IV) and uranium(VI) in a sulphonated cation-exchange resin in aqueous hydrochloric acid[55]. A solution of uranium(VI) in 1.0 *N* hydrochloric acid flowed upwards into a column in contact with cation-exchange resin granules saturated with uranium(IV), when a certain quantity of uranium(VI) ions remained in the resin. After equilibrium had been established in this counterflow contact, the concentration of uranium-235 in the uranium(VI) solution

had increased by a factor of 1.00035 (the initial concentration was arbitrarily taken to be unity), while its concentration in the uranium(IV) sorbed on the exchanger had decreased by a factor 1/1.00035 = 0.99964. Thus the isotopic exchange constant was

$$K = \frac{^{235}U^{VI}_{soln}}{^{235}U^{IV}_{res}} = \frac{1.00035}{0.99964} = 1.0007$$

at every stage of exchange. After the first contact the 235-enriched uranium(VI) solution was reduced with zinc dust to the quadrivalent state; the product was sorbed on a fresh portion of exchanger in a special column, from which the uranium(IV)-saturated granules entered the second stage of exchange. This stage increased the concentration of uranium-235(VI) in the solution to 1.00035 × 1.00035 = 1.0007, but the concentration of uranium-235(IV) in the resin remained at 1.00035 × 0.99964 = 1. In the next stage the concentration of uranium-235(VI) in solution increased to 1.0007 × 1.00035 = 1.00105, while that of uranium-235(IV) in the resin was 1.0007 × 0.99964 = 1.00034; and so on. Therefore the concentration of uranium-235(VI) gradually increased in the solution leaving the top of the exchange column. The quadrivalent uranium present in the resin discharged from the bottom of the column was oxidised with 1% aqueous hydrogen peroxide to the sexivalent state; uranium(VI) was eluted with 0.5 *N* hydrochloric acid. Oxidation and elution could be combined into a single stage by applying the oxidant and the desorbing solution simultaneously.

An alternative procedure is to combine oxidation and the maintenance of uranium(VI) in the system in the same apparatus. The uranium(IV)-saturated resin then passes down the column as in the previous case, while the oxidant (1% hydrogen peroxide) flows upwards together with the eluant. As a result the resin is converted into the hydrogen form and is discharged at the bottom of the column, while the desorbed solution of uranium(VI) moves upwards in contact with resin granules saturated with uranium(IV); the accompanying isotopic exchange leads to enrichment with uranium-235 of the solution of uranium(IV) emerging from the upper part of the column.

A cascade enrichment scheme, entailing the use of several ion-exchange columns, was proposed on the basis of the above variants. The uranium(VI) feed solution enters the middle of the ion-exchange column and moves upwards in contact with resin granules saturated with uranium(IV). Part of the solution leaving the top of the column is led to a special apparatus for the reduction of uranium(VI), and the resulting uranium(IV) is used to saturate a fresh portion of resin, which is returned to the ion-exchange apparatus and moves downwards, meeting the uranium(VI) solution obtained by oxidative desorption of the resin at the next stage of the enrichment process. The other part of the solution leaving the top of the column is fed to the next ion-exchange column. Thus each ion-exchange column within the cascade is fed by admitting near its midpoint a portion of the uranium(VI) solution emerging from the top of the ion-exchange column of the preceding stage and a portion of the uranium(VI) solution obtained by oxidative desorption in the next stage. A uranium solution enriched with the heavy isotope is obtained from the bottom of the ion-exchange column at one end of the cascade, and a solution enriched with the light isotope from the top of the column at the other end.

Interesting experiments aimed at intensifying the isotopic effect in a cation-exchange resin immersed in a hydrochloric-acid solution of uranium were made by Shimokawa and Kobayashi[56], who fed iron(III) chloride solution to a column filled with the resin saturated with uranium(IV). The latter underwent oxidation to uranium(VI), after which uranyl ions were eluted from the resin:

$$3\,R_4U^{IV} + 10\,FeCl_3 + 6\,H_2O \rightleftarrows 3\,U^{VI}O_2Cl_2 + 4\,R_3Fe^{III} + 6\,FeCl_2 + 12\,HCl \quad . \qquad (38)$$

The change in valency of the uranium is expressed by the electron exchange

$$U^{IV} + 2\,Fe^{III} \rightleftarrows U^{VI} + 2\,F^{II} \quad . \qquad (39)$$

The UO_2^{2+} and Fe^{2+} ions are rapidly eluted from the column on the arrival of fresh portions of iron(III) chloride, because the affinity of the cations for the resin varies in the sequence

$$Fe^{3+},\ U^{IV} > UO_2^{2+},\ Fe^{2+} > H^+ \quad .$$

The rates of the chemical reactions and of elution are so large that a very sharp band is formed between the iron(III) and uranium(IV) forms of the exchanger. This band moves at a constant speed determined by the quantity of uranium(IV) sorbed initially and by the concentration and the rate of supply of iron(III) chloride. The process is shown diagrammatically in Fig. 3. During the initial period of operation of the column some of the eluted uranyl ions penetrate the uranium(IV) form of the resin and exchange with hydrogen ions of the latter. After the equilibrium partition of uranyl ions between resin and solution has been established, the concentration of uranyl ions in the eluate becomes constant: uranium(IV) is firmly retained in the band.

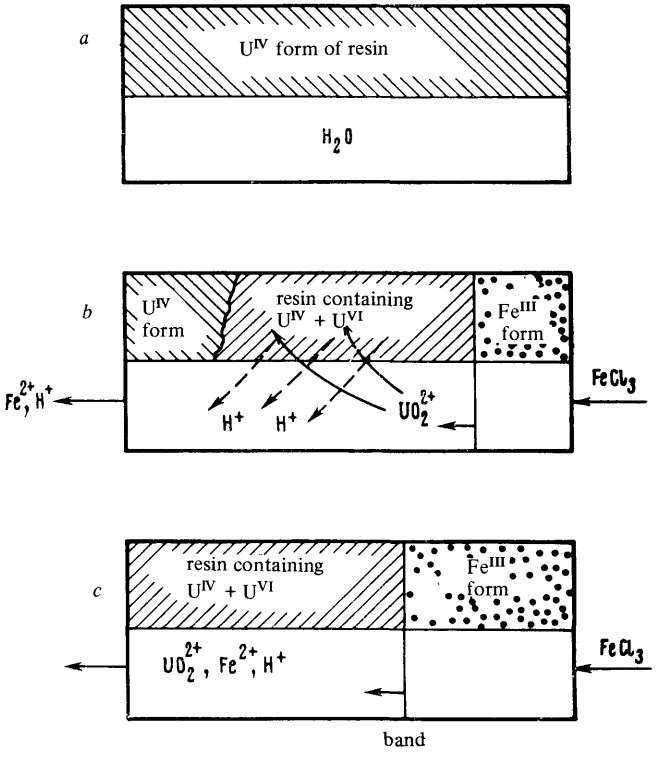


Figure 3. Diagram of movement of band: *a*) before supply of solution; *b*) during initial period of operation of column; *c*) after equilibrium distribution of UO_2^{2+} has been established.

These workers[56] reckoned on strengthening the isotopic effect firstly by the chemical reactions occurring as the band moved along the column and secondly by electron exchange between the two valency states of uranium. The equilibrium constant of isotopic exchange in these experiments was 1.0004–1.0006, regarded as relatively high. It had been reported[57] that such an equilibrium constant should be higher at low temperatures. But the above experiments at 3°C revealed no appreciable fractionating effect; at 20 and 40°C the equilibrium constant of isotopic exchange was respectively 1.0005 and 1.0006.

(*c*) Separation of Uranium Isotopes by Means of an Anion-exchange Resin

Kakihana et al.[58] used Dowex 2 × 10 (100–200 mesh) in the chloride form, in a column of height 100 cm and diameter 1.2 cm, together with solutions in concentrated (8 *N*) hydrochloric acid containing uranium(IV), uranium(VI), and a mixture thereof, flowing at 16 ml h^{-1}. Frontal analysis showed that the separation factor of 0.9993 for solutions containing only uranium(IV) was higher than the value for the mixed solutions (0.9992–0.9986), which can be attributed to the strong influence of the electron exchanges described by Eqn. (19). Indeed, all the experimental results agreed well with theoretical values obtained from Eqn. (35) on the assumption that $K_e = 1.002$.

In 1968 Gonda and Kakihana published experimental results on the fractionation of uranium isotopes in an anion-exchange resin immersed in benzene solutions of trioctylamine and tributyl phosphate[59]. Frontal analysis was used to investigate isotopic exchange for four solutions containing natural uranium (0.72% of uranium-235)— (i) 0.05 M solution of trioctylamine in benzene saturated with uranium(IV), (ii) a mixture of 0.05 M solutions of trioctylamine in benzene saturated respectively with uranium(IV) and uranium(VI), (iii) 0.05 M solution of tributyl phosphate in benzene saturated with uranium(IV), and (iv) a mixture of 0.05 M solutions of tributyl phosphate in benzene saturated respectively with uranium(IV) and with uranium(VI). An ion-exchange column of height 100 cm and diameter 1.3 cm was filled with Dowex 21K (50–100 mesh). Solutions were passed through at 25 ml h^{-1} until the uranium solution had the same composition leaving and entering the column.

In the benzene solution of tributyl phosphate saturated with a mixture of uranium(IV) and uranium(VI) the first samples of eluate obtained on determining the elution sorption curve contained uranium enriched with the lighter isotope (0.732%), by a factor of 1.017 relative to the natural content. This indicates that in this system uranium-238 is more readily sorbed than is uranium-235. The single-stage factor for a solution containing a mixture of valency states was 0.99988, and that for a solution containing only quadrivalent uranium was 0.99989.

The first eluate samples obtained for the elution curve in a benzene solution of trioctylamine saturated with the mixture of valency states were impoverished with respect to the lighter isotope (0.710%, by a factor of 0.987). Hence uranium-235 is more easily sorbed than uranium-238 from a benzene solution of trioctylamine; the single-stage separation factor for this system is 1.00033.

The complete absence of any isotopic effect in the trioctylamine–benzene system saturated only with quadrivalent uranium is due to the similarity in the binding of the latter in the anion-exchange resin and in the solution.

From the above mass-spectrometric results and the fact that uranium(VI) exhibits the greater affinity for the anion-exchange resin in the benzene–tributyl phosphate system, whereas quadrivalent uranium has the greater affinity in benzene–trioctylamine solutions, it was concluded that uranium-235 is concentrated in the quadrivalent state. This is consistent with results for an anion exchanger in 8 M hydrochloric acid containing the mixed valency states[58]. The equilibrium constants of electron exchange in 0.05 M solutions of trioctylamine and of tributyl phosphate in benzene are respectively 1.0010 and 1.0013, both smaller than the equilibrium constant (1.002) in 8 M hydrochloric acid.

3. SEPARATION OF URANIUM ISOTOPES ON A CATION-EXCHANGE RESIN IN A URANYL SALT SOLUTION

Ciric and Zmbov[60,61] studied the separation of uranium isotopes during ion exchange on a cation-exchange resin in an aqueous solution of a uranyl salt. The columns used (l = 1–2 m with S = 0.5 or 1.5 cm^2) were filled with Dowex 50 × 8 or Amberlite IR-120 resin (size of granules 100–200 mesh or 0.1–0.2 mm respectively). The enrichment coefficient was determined by frontal analysis with the application of Glueckauf's equation[62]

$$\varepsilon = \frac{\pi\eta^2}{4\bar{v}s'}\left(1+\frac{\pi\eta}{4}+\frac{5\pi^2\eta^2}{64}+\ldots\right), \qquad (40)$$

where $\eta = (N_0 - N)/N_0$ is the relative enrichment of the more strongly adsorbed isotope in the sample, s' is the gradient of relative enrichment in the sample, $\bar{v}$ is the volume of the sample, and $\epsilon = \alpha - 1$, in which α is the separation factor. We can also apply Spedding's equation[18]

$$\varepsilon = \frac{\sum_{i=1}^{m} V_i C_i (N_0 - N_i)}{QN_0(1-N_0)}, \qquad (41)$$

where V_i, C_i, and N_i are respectively volume, concentration, and content of the more strongly adsorbed isotope in the sample, and Q is the quantity of resin (in equivalents) traversed by the front. Experiments were made with solutions of uranyl nitrate, chloride, and sulphate.

Table 1. Experimental determination of separation factor in systems containing various uranyl salts.

Cation exchanger	Column	Solution		α
		uranyl salt	concn., M	
Amberlite IR-120	l=2 m S=0.5 cm^2	$UO_2(NO_3)_2$	0.3	1.00015±0.00005
		$UO_2(NO_3)_2$	1.0	1.00010±0.00005
		$UO_2(NO_3)_2$	2.0	1.00017±0.00005
		$UO_2(NO_3)_2$	4.0	1.00010±0.00005
Dowex 50 × 8	l=1 m S=1.5 cm^2	$UO_2(NO_3)_2$	2.0	1.0005±0.0002
		UO_2Cl_2	1.0	1.0004±0.0001
		UO_2Cl_2	2.0	1.0006±0.0002
		$UO_2(ClO_4)_2$	1.0	1.0006±0.0001
		UO_2SO_4	2.0	1.00004
		UO_2-tartrate	0.2	.00000

The experimental results show (Table 1) that the separation factor $\alpha = (^{238}U/^{235}U)_{soln}/(^{238}U/^{235}U)_{res}$ varies from unity to 1.0006. The effect of the uranyl salt concentration on the separation factor lies within the limits

of experimental error. The isotopic effect obtained with uranyl nitrate, chloride, and perchlorate is due solely to the ion-exchange reaction[53]

$$^{238}UO_{2\,soln}^{2+} + {}^{238}UO_{2\,res}^{2+} \rightleftarrows {}^{238}UO_{2\,soln}^{2+} + {}^{235}UO_{2\,res}^{2+} \quad . \qquad (42)$$

The strongly hydrated heavier isotope concentrates in the solution, and the lighter isotope in the resin. Lower values were obtained for uranyl sulphate and tartrate, owing to the isotopic effect of the reaction

$$^{235}UO_2^{2+} + {}^{238}UO_2A \rightleftarrows {}^{238}UO_2^{2+} + {}^{235}UO_2A \quad , \qquad (43)$$

where A is an anion forming a complex with the uranyl ion, which partly or completely nullifies the isotopic effect of reaction (42).

4. SEPARATION OF URANIUM ISOTOPES BY A MOVING BAND

Ciric and Zmbov[60,61] used a moving band with non-spreading boundaries, often termed also Spedding's method, to increase the separation of uranium isotopes. The method consists essentially in the movement of a band of constant length through a system of interconnected ion-exchange columns. This procedure enabled Spedding et al.[18] to achieve complete separation of macroquantities of nitrogen isotopes.

The uranyl band can be moved in a cation-exchange resin in two ways: (*a*) a solution containing a doubly charged cation having greater affinity for the exchanger than has the uranyl ion is used to advance the uranyl band in a column filled with Dowex 50 × 8 in the hydrogen form (choice of a suitable cation presents no special difficulty[63]); or (*b*) the band is moved by means of solutions of salts of weak acids whose anions form stable uranyl complexes. In the elution of a uranyl band with an ammonium acetate buffer, for example, the desorption equilibrium

$$2(NH_4^+)_{soln} + (HAc)_{soln} + 2(Ac^-)_{soln} + UO_{2\,res}^{2+} \rightleftharpoons 2(NH_4^+)_{res} + ([UO_2Ac_3]^-)_{soln} + (H^+)_{soln} \qquad (44)$$

and the adsorption equilibrium

$$(H^+)_{soln} + [(UO_2Ac_3^-]_{soln} + 2(H^+)_{res} \rightleftharpoons UO_{2\,res}^{2+} + 3(HAc)_{soln} \qquad (45)$$

are displaced considerably to the right in the lower part of a column filled with the resin in the hydrogen form. As a consequence, both edges of the band are very sharp, so that its length remains constant during elution. Ammonium acetate can be replaced by the citrate, glycollate, lactate, or other ammonium salts.

Table 2.

Cation exchanger	α
Amberlite IR-120	1.00016±0.00005
Dowex 50 × 8	1.0004±0.00001

The original experiments were made in columns (1 m × 0.5 cm^2) filled with Amberlite IR-120 or Dowex 50 × 8, with ammonium citrate solution (0.29 M of pH 4.4) as eluant. The length of the band was 4 cm. The separation factor α was determined by means of Glueckauf's[19] and Spedding's[18] equations, and the results are listed in Table 2.

The next experiment used columns (S = 1.5 cm^2) of Dowex 50 × 8 cation-exchange resin connected in series. The band length was 11 cm with the same eluant. The experiment was terminated after the band had travelled 6.5 m at 10 cm h^{-1}. The uranium-235 content changed from 0.670% in the first few samples to 0.740% in the last sample. An experiment using the same eluant with a band length of 54 cm was terminated after a travel of 14 m. Although the system was far from equilibrium, the uranium-235 content in the last sample was 0.760%.

In another case the initial band length was 8 cm (actually 11 cm because of the slope of leading and trailing edges), elution was effected by ammonium citrate (0.25 M of pH 4.95), and the experiment was stopped after the band had travelled 1.5 m at 3 cm h^{-1}. The uranium-235 contents in first and last samples were 0.640 ± 0.010% and 0.744 ± 0.005%, with α = 1.0004 ± 0.0001.

The experiments described above show that Dowex 50 × 8 gives higher values than does Amberlite IR-120.

5. SEPARATION OF ISOTOPES IN AN ION-EXCHANGE COLUMN WITH APPLICATION OF AN ELECTRIC FIELD

In 1950 some Japanese workers were successful in separating copper and nickel isotopes by applying a constant electric field to an ion-exchange resin. Since then repeated attempts have been made to use ion exchangers to separate isotopes of various elements by electromigration[64-69].

Table 3. Enrichment with uranium-235 by electromigration.

Duration of electromigration, h	400	600	1000
Isotopic ^{235}U content in anodic compartment, %	0.709±0.004	0.715±0.004	0.720±0.007
Quantity of ^{235}U remaining in anodic compartment, mg	728	63	4

The effect produced by applying an alternating electric field was described by Japanese scientists in a paper at the Third International Conference on the Peaceful Uses of Atomic Energy[13]. A borosilicate glass vessel was used, divided by cation-exchange membranes into several compartments. One end compartment was filled with ammonium chloride solution to separate the nitrogen isotopes and to serve as anolyte, while the cathode compartment at the other end was filled with aqueous hydrochloric acid; all the intermediate compartments were filled with a cation-exchange resin. Ion-exchange electromigration of ammonium ions was accomplished by applying an alternating current, when the ammonium ion passed through the cation-exchange resin from anode to cathode, changing the direction of its motion with variation in the a.c. phase. The above experiment showed that the heavier isotope nitrogen-15 reaches the cathode compartment more rapidly than does the lighter isotope nitrogen-14.

This method has been used with the same apparatus for the enrichment of uranium-235, whose content in the initial sample of uranyl nitrate was 0.702 ± 0.005%. Amberlite IR-120 of type 2 (in the hydrogen form) was

used, of diameter 2 cm and length 75 cm; the anodic compartment contained 40 ml of 0.5 M uranyl nitrate solution and the cathodic compartment 40 ml of 0.5 M nitric acid. The results are listed in Table 3. This method may give good results[13] in the enrichment of uranium isotopes.

6. Separation of Uranium Isotopes by Electromigration

Cation-exchange membranes are effective for the separation of lithium isotopes[66], and appreciable enrichment has been observed also with uranium. The use of ion-exchange membranes is attractive because the solvation (or hydration) of isotopic ions is far less in them than in solution. This means that the difference in mass between isotopes may have a greater effect on separation in a membrane than in solution. This method has proved most effective for the separation of lithium isotopes in comparison with potassium, copper, and uranium isotopes[70]. The single-stage separation factor for uranium-235 and uranium-238 was 1.00006.

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Thermal Decomposition of Solid Metal Oxides

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Certain aspects of the kinetics and mechanism of the thermal dissociation of solid metal oxides are considered, and two types of decomposition differing in mechanism—radical and molecular—are discussed. The possibility of elucidating characteristic features of these types of dissociation is analysed. A list of 81 references is included.

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I. INTRODUCTION

The attention paid by research workers to the thermal dissociation of solid metal oxides is due primarily to the fact that such reactions, together with the dissociation of carbonates and sulphides, form, in Rostovtsev's descriptive expression[1], "a kind of cornerstone of the thermodynamic study of metallurgical processes". A fairly comprehensive literature has appeared on the thermodynamics of the thermolysis of metal oxides (see e.g. the monographs[1-4] and the references in them).

Far fewer kinetic studies have been made on the thermal decomposition of solid oxides. Yet investigation of the formal kinetics and detailed examination of the mechanism of these reactions is important for several reasons. Firstly, establishment of the fundamental kinetics of the thermolysis of solid metal oxides may be of practical value, since it is probable that such processes largely determine the chemistry of the thermal reduction with carbon of many readily dissociated oxides[5-9]. Secondly, the condensate dissociation (Kulikov's term[2]) of oxides belongs to the broad class of reactions

$$A(solid) = B(solid) + C(gas). \quad (1)$$

Investigation of the decomposition of oxides may be expected to clarify many features of such reactions, such as "nucleation", the autocatalytic effect, etc. Here it is noteworthy that, because the volume relations of the initial higher oxides do not greatly differ from those of the oxide products[10], pore formation, which usually complicates the investigation of topochemical reactions[11], has no marked effect. (An original technique permitting extremely delicate monitoring of the variation in the degree of dispersion of metal oxides during various redox reactions has recently been developed by Mardaleishvili et al.[12-14]) Thirdly, the kinetic behaviour of a substance reflects its intrinsic properties. Study of the kinetics of the decomposition of solid oxides and its mechanism will permit a deeper insight into the nature and structure of these compounds.

A most comprehensive survey of kinetic problems of the dissociation of metal oxides was made by Esin and Gel'd[4]. Garner[15] and Young[16] made detailed analyses of experimental results on the thermolysis of silver oxide.

II. FORMAL KINETIC INVESTIGATIONS OF THE THERMAL DECOMPOSITION OF METAL OXIDES

Until recently the kinetics and the mechanism of the thermal dissociation of oxides were investigated almost solely by the formal kinetic method, which consists essentially in finding the time dependence of the reaction velocity, and hence reaching conclusions on the reaction mechanism. Many formal kinetic equations, deduced from very different views on the mechanism of the processes, were suggested to describe the course of the heterogeneous decomposition of solids. Pavlyuchenko[17] reckoned that about forty such equations had been proposed. Kinetic investigation of the thermal decomposition of oxides and solids in general can be regarded as originating in 1905 with the work of Lewis on the thermolysis of silver oxide[18]. He gave a kinetic equation and attempted to explain the mechanism of the reaction.

Formal kinetic investigations have now been made on the decomposition of the oxides of silver[18-25], manganese[5,6,26], copper[8], terbium and praseodymium[27,28], chromium[29], lead[9,30-32], cobalt[7], and uranium[33-39]. Several of these papers, in particular those of Rostovtsev and his coworkers, as well as certain papers by Vlasov and Beketov, do not give formal kinetic equations for the reactions investigated, although they do contain graphs illustrating the dependence of reaction velocity on degree of conversion.

Investigations on the dissociation and the reduction of manganese and copper oxides, of great importance for the theory of metallurgy, were made under the direction of Chufarov[40-42]. Unfortunately, no quantitative data on the formal kinetics of the reactions were given, although indications appeared of their topochemical character. The effects of temperature and oxygen pressure on the rate of decomposition of the oxides were traced, and activation energies determined for the thermolysis of manganese dioxide, manganese sesquioxide, and copper(II) oxide.

Several conclusions can be reached from a general analysis of experimental data on the formal kinetics of the thermal decomposition of solid metal oxides.

If the range of homogeneity of the initial higher oxide is sufficiently wide, the decomposition curves obey the equations of diffusion kinetics within this region. For example, the thermolyses of $PrO_{1.72-y}$ and U_3O_{8-y} [29,38] are well described by the equation

$$\frac{X_0 - X}{X_0 - X_\infty} = 1 - \frac{6}{\pi^2}\sum_{n=1}^{\infty}\frac{1}{n^2}\exp\left(-\frac{n^2\pi^2 Dt}{R^2}\right) , \quad (2)$$

where R is the radius of a spherical oxide particle, t is the duration of the experiment, and X_0, X, and X_∞ are the quantities of oxygen in the oxide initially, at moment t, and after an infinite time respectively. The postulates made in deducing this equation—that the specimen consists of spherical particles of the same radius, that equilibrium corresponding to the final composition of the oxide is rapidly established at the solid–gas interface, and that the diffusion coefficient is independent of X—are obviously not too crude. This work[29,38] enables the relative ease with which oxygen atoms move through the oxide lattices to be assessed: the activation energy for the diffusion of oxygen in $PrO_{1.72-y}$ and in U_3O_{8-y} is respectively 42 and 45 kcal mole^{-1}.

In spite of the apparent complexity, treatment of experimental results by means of Eqn. (2) presents no great difficulty. The dependence of $\lg(X - X_\infty)$ on time when t is large should be linear with a slope of $-\pi^2 D/2.3R^2$. Having evaluated this quantity, we can easily plot the curve even at small values of t, and with R known, e.g. from measurements of specific surface, we can calculate the diffusion coefficient. It is therefore often inadvisable to use various simplified forms of the diffusion equation, e.g. the equation[43-45]

$$\alpha = kt^{1/n} , \quad (3)$$

where α is the degree of conversion and k the specific rate constant.

When the ranges of homogeneity of initial and final oxides are narrow, the decomposition curves are described by extremely diverse equations of topochemical kinetics. The most usual[27,28,30,31] is the "contractile sphere" equation deduced by Roginskii and Shul'ts[46]. The experimental results satisfy the same kinetic equation for a fairly wide range of degrees of conversion, which, from our point of view, underlines the near invariability of the state of aggregation of the substances. Cracking of the fine oxide crystals is improbable, because the volume relations of initial and final oxides do not markedly differ. Nor should sintering greatly complicate the observed pattern, since kinetic examination of the decomposition of oxides is usually made in an inert atmosphere or in a vacuum at moderate temperatures.

Deviations from the curve at low degrees of conversion are due both to the complexity of nucleation processes[15,16,32] and to the possible occurrence of decomposition within the range of homogeneity of the initial higher oxide[26]. The slowing down of the reaction at high degrees of conversion probably has several causes, e.g. the formation of a dense layer of reaction products, through which oxygen must diffuse. Furthermore, dissociation may then occur within the range of homogeneity of the final oxide. An example of such behaviour is the decomposition of higher oxides of uranium to U_3O_{8+x}, the upper limit of which probably extends to the composition $UO_{2.76}$.[47]

Thus the kinetics of the thermolysis of oxides, while having much in common with other reactions of type (1), possesses its peculiarities resulting from the wide dissemination of non-stoichiometric compounds among the oxides.

III. CLASSIFICATION OF THE THERMAL DISSOCIATION OF METAL OXIDES

The mechanism of the dissociation of solid metal oxides is usually regarded as comprising the stages—"(i) formation of oxygen atoms adsorbed at the interface, (ii) their combination to molecules, (iii) desorption of oxygen molecules, and (iv) formation and growth of nuclei of a new phase"[4]—among which Lewis[18] assumed (ii) to be the slowest. Breakdown of the initial higher oxide is now regarded as meeting this criterion.

However, several experimental facts are inconsistent with this simple scheme[48]. Thus because the structure of the transition complex is closely similar to that of the reaction products of an endothermic reaction[49,50], for example, the activation energy of the thermal decomposition of oxides should, according to the above scheme, be similar in magnitude to the heat of reaction

$$M_nO_x \rightarrow M_nO_{x-1} + [O](\text{solid}) , \quad (4)$$

where [O](solid) represents an oxygen atom adsorbed at the interface between initial and final oxides. The energy of interaction of such an atom with the matrix of the solid oxide is difficult to determine, but obviously the heat of reaction (4) should not greatly differ from the heat of reaction

$$M_nO_x \rightarrow M_nO_{x-1} + O(\text{gas}) , \quad (5)$$

which can easily be calculated from tabulated enthalpies of formation. The heat of reaction (5) for oxides undergoing decomposition is usually considerably greater (by 40–50 kcal mole^{-1}) than the heat of reaction

$$2M_nO_x \rightarrow 2M_nO_{x-1} + O_2 . \quad (6)$$

Experimental activation energies of the thermal condensate dissociation of oxides are usually closely similar to the heat of reaction (6), and in any case considerably smaller than the heat of reaction (5)[5-9,18-42].

The reason why this discrepancy was ignored for such a long time probably lies in the history of the development of kinetic investigations. Lewis's early work on the decomposition of silver oxide was followed by a fairly lengthy period (until the end of the 1940s) during which the kinetics of the dissociation of oxides remained almost uninvestigated. But very sound kinetic studies were made during this time on the decomposition of carbonates and hydrates[4,15,16], which showed that in the majority of cases the activation energy of these reactions was equal to the heat of reaction (1) with C representing the CO_2 or H_2O formed. This result is entirely consistent with the theory of the activated complex. By the start of the new period in the kinetic investigation of the thermal dissociation of oxides the view had already become deeply rooted that full identity existed between the decomposition of oxides and the thermolysis of carbonates and hydrates. Since molecular oxygen is an end-product of the former reaction, it was accepted as entirely natural, by analogy with the latter[26], that the activation energy should coincide with the heat of reaction (6).

There remains at least one further extremely interesting problem—the irreversibility of the thermal decomposition of certain oxides—which probably cannot be solved in terms of the existing model. This is of some practical importance, since the irreversibility observed with several higher oxides casts doubt on the significance of determinations of their dissociation pressures, e.g. of oxides of lead[51], manganese[52], and uranium[53].

In view of all the above considerations, further development of the theory of the thermal dissociation of solid metal oxides is obviously necessary on the basis of fresh experimental results.

A very useful method for elucidating the mechanism of a complicated process is to record the reaction intermediates; it has been widely employed in the kinetic investigation of homogeneous chemical reactions [54-56]. Atomic oxygen has recently been increasingly widely recorded as intermediate in several cases of the thermal decomposition of solids, including oxides [30-32,39,48,57-61]. Experiments have shown that the thermal dissociation of some oxides is accompanied by the evolution only of molecular oxygen, whereas both atomic and molecular varieties are evolved in the thermolysis of other oxides. Furthermore, the latter decompositions were found to be reversible, whereas those accompanied by the evolution only of molecular oxygen were irreversible [31,32,39,48,60,61]. (The possibility of the evolution of atomic oxygen in the thermal decomposition of certain solid metal oxides was probably first mentioned by Baikov and Tumarev in 1937. [62] It is interesting that their results are somewhat similar to those just mentioned. These workers found that oxides which were reduced irreversibly by carbon monoxide evolved almost pure carbon dioxide on reaction with carbon, whereas other oxides gave a nearly equilibrium mixture of the monoxide and the dioxide.)

It was proposed [48] that the differences in the behaviour of solid oxides should be used to classify their thermal decomposition into two types, according as both atomic and molecular oxygen or only the latter is evolved. It is noteworthy that the kinetic parameters (activation energy and pre-exponential factor) determined in oxygen (air) usually differ markedly for these two types of reaction. Available data indicate that the first type includes the thermal decompositions $Pb_3O_4 \rightarrow PbO$, $Co_3O_4 \rightarrow CoO$, α-$PbO_x \rightarrow \beta$-PbO_x, $U_3O_8 \rightarrow U_8O_{21}$, $UO_{2+x} \rightarrow UO_{2.00}$, and $CuO \rightarrow Cu_2O$; and the second type includes β-$PbO_2 \rightarrow \alpha$-PbO_x, $Ag_2O \rightarrow Ag$, α-$PbO_x \rightarrow Pb_3O_4$, α-$PbO_2 \rightarrow \alpha$-PbO_x, $UO_3 \rightarrow UO_{2.9}$, $UO_{2.9} \rightarrow U_3O_8$, ϵ-$UO_3 \rightarrow U_3O_8$, $CrO_2 \rightarrow Cr_2O_3$, β-$MnO_2 \rightarrow \alpha$-Mn_2O_3, and α-$Mn_2O_3 \rightarrow \beta$-$Mn_3O_4$. Harano's experiments [57,58] indicated that atomic oxygen was evolved in the thermal dissociation of HgO, ZnO, and PtO_2.

Since the percentage of atomic oxygen in the gas evolved in the thermal decomposition of oxides of the first type is quite high [32], these reactions can well be regarded as a simple method for generating atomic oxygen. The results discussed may have some applied value, since work is now being widely undertaken on the use of oxygen from metal oxides for oxidising fuels [63].

IV. MECHANISMS OF THE TWO TYPES OF DISSOCIATION OF OXIDES

Since the first type of thermal decomposition of oxides involves the evolution of both atomic and molecular oxygen, whereas the second type gives only molecular oxygen, it was suggested [30,48] that the reaction mechanism of the former is similar to that generally accepted, whereas the latter has a different mechanism. Molecular oxygen is evidently formed directly by breakdown of the initial higher oxide in the latter type. This provides a natural explanation of the similarity of the activation energy to the heat of reaction (6) observed with these reactions.

In order that oxygen [atoms] should leave the oxide lattice in pairs (as molecules) during thermal decomposition of the oxide, interaction should occur between oxygen atoms in the initial lattice. Ignoring the form of interaction (the nature of the chemical bond in oxides is a matter of controversy [64]), we can state that the mutual influence will be stronger the shorter the oxygen–oxygen distance, which is shortest in peroxides. In 1958 Pavlyuchenko and Rubinchik [65] concluded from the activation energies and the heats of reaction of certain peroxides that atomic oxygen was not formed in their thermal breakdown. This was confirmed by Harano's experiments [57] and by other results [60].

In contrast to peroxides, it is difficult in oxides to distinguish any pair of oxygen atoms whose interaction would differ significantly from that with other neighbours. However, it may be questioned how marked this difference should be. No criterion is available at the present time.

Several higher oxides contain comparatively short oxygen–oxygen bonds. In the Reviewers' opinion this indicates the possibility of interaction between such atoms. Thus in β-PbO_2 [66] every four pairs of oxygen atoms distant 3.03 Å apart and one pair with a distance of 3.38 Å are accompanied by a pair 2.67 Å apart. It may be suggested that such a pair is able to behave as a unit during the act of breakdown and form an oxygen molecule. The important factor is not so much the absolute value of the shortest oxygen–oxygen distance as its difference from the mean. The energy of the metal–oxygen bond is obviously also important.

A similar idea to the above has recently been put forward by Porai-Koshits and Atovmyan [67]: from the structure of certain compounds containing oxygen or sulphur they concluded that the shortening of the O...O and S...S distance along an edge common to adjoining MX_6 octahedra is a consequence of the mutual attraction of the non-metal atoms. (The presence of such octahedra, linked in various ways, can be monitored in most higher oxides.) This idea seems the more valid as the explanation of the shortened non-metal–non-metal distance once put forward by Pauling [68] is unconvincing in the light of modern data on the effective charges in oxides and sulphides [64]. The mechanism suggested for reactions of this second type is further supported by work [61] showing, from the topotaxy [69] of the reaction $CrO_2 \rightarrow Cr_2O_3$ and formulation of the principle of minimum rearrangement of the lattice (the maximum possible number of previous bonds are preserved in a reaction), that the CrO_2 lattice can be transformed into the lattice of chromic oxide by removing pairs of oxygen atoms. The pairs thus removed lay on a common edge of adjoining MX_6 octahedra (i.e. they were a comparatively short distance apart).

The mechanism suggested for reactions of the second type is consistent also with their irreversibility. Theoretical examination has shown [70] that, if molecular oxygen is formed immediately on breakdown of the initial higher oxide, it is desirable, for the reverse reaction to occur, that oxygen should reach the interface between initial and final oxides in the form of molecules. However, an oxygen molecule is comparatively large, and its insertion would produce appreciable distortions in the oxide lattice. Hitherto there has been no direct experimental evidence of the possibility of the dissolution of molecular oxygen in oxides [71]. Experimental studies of the introduction of large molecules into the lattices of less rigid substances, e.g. graphite, indicate the presence of large sorption hysteresis [72]. If the pressure is raised considerably above the equilibrium value during a reaction of the second

type, oxidation of the lower oxide is observed, but its rate is extremely low. Thus according to Otto[52] the equilibrium oxygen pressure in the β-MnO_2–α-Mn_2O_3–O_2 system at 475°C is 1.4 atm. By raising the pressure almost hundredfold, he was able to observe partial oxidation of the sesquioxide, but no such oxidation was observed during the first 200 h after the pressure had been raised. Equilibrium oxidation of the sesquioxide would have required a year. The less rigid the lattice of the lower oxide, the more readily should oxidation occur. This will probably explain why several higher oxides of metals, e.g. manganese and uranium, can be obtained by oxidising lower oxides if the latter have been obtained in a finely dispersed or an amorphous state. The thermal decomposition α-$Mn_2O_3 \rightarrow \beta$-$Mn_3O_4$ is very characteristic in this respect. The Reviewers' experiments have shown that only molecular oxygen is evolved. However, several investigators regard the thermal decomposition of manganese sesquioxide as reversible. Summarising the results of many workers, Rabkin et al. concluded[73]: "In some cases the conversion of Mn_2O_3 into Mn_3O_4 is a reversible process depending on temperature and time of heating, as well as on the degree of dispersion. However, prolonged heating at a high temperature leads to the formation of Mn_3O_4 showing no tendency to absorb oxygen."

The problem of the irreversibility of thermal decompositions of oxides of the second type can in general be regarded as solved. A series of crucial experiments should be undertaken. Furthermore, the appearance of many studies on the irreversibility of thermal decomposition of several hydrates and carbonates would have been extremely useful, since these systems can be investigated by improved analytical methods, such as infrared spectroscopy, nuclear magnetic resonance, and isotopic exchange.

As has been mentioned, the mechanism of the first type of thermal decomposition of oxides is probably closely similar to the generally accepted condensate dissociation of solid metal oxides. Since very few investigations have been made on the thermolysis of oxides in which the evolution of atomic oxygen has already been established, it is difficult to analyse the laws governing reactions of this type. Nevertheless, one question can usefully be raised. According to the simple scheme of the decomposition of metal oxides[4], the activation energy of such reactions should differ little from the heat of reaction (5) $\Delta H^{\circ}_{T}(O)$. Let us estimate the latter for a few oxides, for which reliable thermodynamic data are available[2,74]. Since heats of reaction usually vary little with temperature, the calculation was made for 298 K. Thus approximate values of 79, 84, and 94 kcal g-atom^{-1} O have been obtained for $\Delta H^{\circ}_{298}(O)$ for the reactions $Pb_3O_4 = 3PbO + O$, $Co_3O_4 = 3CoO + O$, and $2CuO = Cu_2O + O$ respectively. The activation energy of the thermal decomposition of red lead has been given[32] as $E_a = 45 \pm 15$ kcal mole^{-1}; Ashin and Rostovtsev[7] give $E_a = 70$ kcal mole^{-1} for the thermal dissociation of Co_3O_4, and $E_a = 57$ kcal mole^{-1} for the thermolysis of copper(II) oxide[8], the latter of which compares with the value 49 found by Tatievskaya and Chufarov[42]. (The recalculation of the activation energy for the last reaction based by Esin and Gel'd[4] on the results[42] is probably illegitimate.) Chufarov et al.[40,41] calculated the activation energy from the temperature dependence of reaction velocity at zero oxygen pressure in the system. The rate of decomposition of oxides in an atmosphere of the reactant gas can be written

$$v(T) = k(T)S\overline{(m - m_{\infty})}\left(1 - \frac{p}{P_{O_2}}\right), \qquad (7)$$

where $v(T)$ is the reaction velocity, $k(T)$ the rate constant, S the interfacial area, $(M - m_{\infty})$ the quantity of oxygen removed from unit interfacial area, p the oxygen pressure in the system, and P_{O_2} the equilibrium dissociation pressure at the experimental temperature. We see that $v \rightarrow v_{max}$ as $p \rightarrow 0$, and v_{max} is independent of the equilibrium oxygen pressure. Hence the temperature dependence of v_{max} is determined by that of k: i.e. in the formula

$$v_{max.} = A\exp\left(-\frac{E_a}{RT}\right) \qquad (8)$$

E_a coincides with the activation energy of the rate constant.

Thus the first type of thermal decomposition of oxides evidently exhibits the extremely rare relationship that the activation energy is smaller than the heat of reaction. A similar relation is found also in the thermolysis of mercury(II) oxide[75]. Observed activation energies are usually considerably smaller than heats of reaction also in the thermolysis of metal sulphides with the formation of sulphur atoms[76,77].

This can be explained on the hypothesis adopted by Benson for gas-phase dissociations[78], that products of the individual act of breakdown are formed in a frozen state. An approximate calculation shows that the heat of the non-isothermal reaction

$$Pb_3O_4 \rightarrow (3PbO + O)^{*} \qquad (9)$$

in which red lead is at 823 K, while PbO and O are 550 deg cooler, is smaller by 20 kcal than the heat of the isothermal reaction $Pb_3O_4 \rightarrow 3PbO + O$. Unfortunately, it is difficult to have a detailed picture for solid-phase reactions of the act of breakdown—to estimate the energy of interaction of oxygen atoms with the lattice, to determine the numbers of metal and oxygen atoms involved in a single act, etc.

An alternative explanation may be suggested for this aspect of the first type of dissociation of oxides, that a multistage mechanism is involved. The first stage—breakdown of the initial higher oxide—is strongly endothermic, but a large quantity of energy is evolved by the combination of oxygen atoms to form molecules. The latter energy (~ 5 eV, which is considerably greater than the energy of thermal phonons) may not be immediately disseminated as heat, but may be divided into two quanta each of 2–3 eV and transmitted resonantly to the interface, i.e. to the site of breakdown in the periodicity of the lattice. "Molecules" of the higher oxide situated at the interface are excited. The destruction of such excited states requires, of course, a considerably lower activation energy.

Further experimental work is required before final conclusions can be reached, but the mechanism of the thermal decomposition of metal oxides is in any case more complicated than had hitherto been thought.

Finally, we must bear in mind, when considering the sequence metal–oxides–oxygen, that oxides contain not only the main metal–oxygen bonds determining their nature but also certain other bonds. Metal–metal interaction must be taken into account in the lattices of several unsaturated oxides[79], and oxygen–oxygen interaction in those of higher oxides, the latter being especially pronounced in metal peroxides. Furthermore, some molecular character is present in metal oxides such as alumina and titania, evident in the fact that the metal does not interact in the same way with all the oxygen atoms surrounding it[80,81]. A feature of such oxides is that M_xO_y molecules pass into the gas phase when they are heated.

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Mono-oxygenase Enzymes and Their Simulation

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Information on reactions catalysed by mono-oxygenases is summarised and classified. The composition and properties of these enzymes are considered, together with the kinetics and the mechanism of their action in the hydroxylation of aliphatic and aromatic compounds and in the epoxidation of alkenes. Methods for imitating the action of mono-oxygenases are discussed and systematised, and the reaction mechanisms of the model systems are examined critically. A list of 193 references is included.

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I. INTRODUCTION

It is well known that molecular oxygen is relatively inert, and is unable directly to oxidise amino-acids, steroids, hydrocarbons, and other compounds in living organisms. Indeed, the reaction between an oxygen molecule and a hydrocarbon $RH + O_2 \rightarrow R\cdot + HO_2\cdot$ is strongly endothermic ($Q_{H-O_2} - Q_{R-H} = 47 - 93 = -46$ kcal mole^{-1} [1]) and can occur at a measurable rate only at very high temperatures. Under conditions approximating to biological the oxygen molecule cannot be converted into two active atoms, since the strength of the O=O bond is 117.2 kcal mole^{-1} [1]. Oxygen will become an active oxidant when it undergoes stepwise reduction to the radicals $HO_2\cdot$ and $HO\cdot$ and to hydrogen peroxide. Stepwise reduction of molecular oxygen may take place thermally, radiolytically, or in the concerted oxidation of organic compounds[2]. The active oxidants—H_2O_2, $HO\cdot$, $\cdot O_2H$—operate very non-selectively on substrates, so that a large number of reaction products are formed. Yet micro-organisms are able to assimilate various hydrocarbons and other compounds, and to oxidise them under mild conditions with extraordinary selectivity[3-7]. Such complicated organic molecules as steroids can be transformed selectively into hydroxy-derivatives (hydroxylated) by micro-organisms[8,9]. The hydroxylation of various substrates—amino-acids, steroids, hydrocarbons, heterocyclic compounds, etc. — is one of the most important among physiological processes. It can now be accepted as proved that hydroxylation is accomplished by means of enzyme systems—termed mono-oxygenases--belonging to the class of oxidoreductases. Enzymes of this type, discovered in 1954 by Mason[10-13], have the distinguishing feature that, during reactions which they catalyse, one atom of an oxygen molecule is consumed in oxidising the substrate (S), while the other atom is reduced to water, so that the overall hydroxylation is represented by the equation $S + O_2 + DH_2 \rightarrow SO + H_2O + D$, where DH_2 is the cosubstrate, which is dehydrogenated by the reaction. If the substrate itself acts as cosubstrate ($SH_2 + O_2 \rightarrow SO + H_2O$), the mono-oxygenase is said to be "internal" [14].

Mason himself names the type of enzymes he had discovered "mixed-function oxidases", thereby stressing that the enzymes belonged to the class of oxidases and registering the unusualness of the insertion of oxygen into a substrate. Hayaishi [12-14] suggested the term "mono-oxygenases", which is now widely used, since it enables mono-oxygenases to be distinguished from dioxygenases, which insert two oxygen atoms together into a substrate.

Mono-oxygenase enzymes have recently been intensively studied, and the research results are reflected in several reviews, devoted mainly to biological aspects of the action of mono-oxygenases[4,11,15]. The aim of the present Review is to describe the mono-oxygenases known at the present time, to classify them according to types of reactions and structure, to assess their role in biological oxidation, and to discuss their composition and properties. We would like to lay special emphasis on the role of models in the study of the mechanism of reactions catalysed by mono-oxygenases. We have considered mainly recent papers, since they provide the newest information and cover that obtained earlier. Generally accepted biochemical abbreviations are used in the Review.

II. OCCURRENCE, SITE AND ROLE OF MONO-OXYGENASES IN BIOLOGICAL OXIDATION

All intracellular respiratory processes can be divided into two classes—(i) oxidation associated with the accumulation of energy and (ii) free oxidation, unconnected with the formation of high-energy (macroergic) compounds. Concerted phosphorylating oxidation provides an energy supply for the cell and is affected by means of a poly-enzymic complex whose structure is completely obscure. This complex consists of several electron carriers, whose reduction potentials at pH 7.0 lie between those of the initial donor (NAD–NADH = −0.320 V) and the final acceptor (O_2–H_2O = 0.815 V). Thus a large potential difference arises, and the initial energy of oxidation of the substrate is involved in the process. This energy is partly (~40%) consumed in forming adenosine triphosphate.

The energy of hydrolysis of ATP is used by the cell in biosynthetic reactions, which otherwise would be thermodynamically disadvantageous. The role of oxygen in concerted oxidation is to accept electrons liberated by dehydrogenation. Degradative metabolism in the cell and this function of oxygen are now quite well known, and are described in detail in handbooks of biological chemistry[16].

Free oxidation, unconnected with the formation of high-energy compounds, is effected by means of enzymes, which can be divided into two classes—oxidases and oxygenases—but proteins—the oxygen carriers haemoglobin, myoglobin, and haemocyanin—are excluded from consideration. Oxidases are dehydrogenases, using oxygen as electron acceptor and reducing it to hydrogen peroxide[17]. Depending on the nature of the prosthetic groups oxidases are flavoproteins, metal flavoproteins, or copper proteins.

Table 1. The most studied mono-oxygenases.

Enzyme	Electron donor	Occurrence	Ref.
steroid mono-oxygenases			
Squalene 2,3-mono-oxygenase EC 1.12.1.3	NADPH	liver	28, 29
11β-Mono-oxygenase EC 1.14.1.6	NADPH	adrenal mitochondria	30—32
$C_{(21)}$-Mono-oxygenase EC 1.14.1.8	NADPH	adrenal-gland endoplasmic retirulum	33, 34
Cholesterol 20-mono-oxygenase EC 1.14.1.9	NADPH	adrenal mitochondria	35, 36
1α, 1β, 2β, 6α, 6β, 7α, 7β, 15α, 16α, 18α-Mono-oxygenase	NADPH	liver endoplasmic reticulum	37—40
Mono-oxygenases of amino-acids and their derivatives			
L-Kynurenine 3-mono-oxygenase EC 1.14.1.2	NADPH NADH	liver mitochondria	41, 42
Dopamine β-mono-oxygenase EC 1.14.2.1	ascorbate	adrenal glands	43, 44
p-Hydroxyphenylpyruvate 1-mono-oxygenase EC 1.14.2.2	aldehyde formed	liver cytoplasm	45, 46
Phenylalanine 4-mono-oxygenase EC 1.14.3.1	tetrahydrobiopterin	liver cytoplasm	47, 48
Proline 4-mono-oxygenase	ascorbate		49, 50
other mono-oxygenases			
gem-α-Mono-oxygenase	NADPH	liver endoplasmic reticulum	51
Aliphatic-acid ω-oxygenase	NADPH	liver endoplasmic reticulum	52—54
Arene *p*-mono-oxygenase	NADPH	liver endoplasmic reticulum	55, 56
Alkane mono-oxygenase	NADPH	liver endoplasmic reticulum	53, 57—59
p-Hydroxybenzoate hydroxylase EC 1.14.1.12	NADPH	*Pseudomonas desmolytica*	60
Camphor 5-mono-oxygenase	NADPH	*Pseudomonas putida*	61, 62

In contrast to oxidases, oxygenases catalyse reactions during which oxygen combines with the substrate. If one oxygen atom is attached, the enzyme is a mono-oxygenase; if two oxygen atoms are introduced into the substrate, the enzyme is termed a dioxygenase. As already noted, one oxygen atom is consumed in oxidising the substrate in the actions catalysed by mono-oxygenases, while the other oxygen atom is reduced to water. It is the latter atom which serves as electron acceptor, as with oxidases. This explains the term "mixed-function oxidase". This function of oxidases requires the presence of a cosubstrate, which undergoes dehydrogenation during the reaction. If the substrate itself acts as cosubstrate, the enzyme is termed an internal mono-oxygenase. Thus mono-oxygenase enzymes catalyse reactions in which the role of oxygen is not restricted to serving as electron acceptor but involves incorporation into the substrate, i.e. oxidation of the latter. Examples of internal mono-oxygenases are—lysine oxygenase[14,18], lactate decarboxylase[19], tryptophan oxygenase[20], and arginine oxygenase[21].

Reactions catalysed by mono-oxygenases are widely represented in biological systems. A special respiratory chain comprising free-oxidation enzymes is localised in microsomes in the liver, where most foreign compounds and several natural metabolites undergo transformations leading to non-toxic polar products, which are then excreted by the kidneys. The mono-oxygenase-catalysed hydroxylation of medicinal, carcinogenic, and toxic substances is of great interest for pharmacology, oncology, and toxicology[4,22]. A hydroxylation chain similar in composition to the microsomal chain functions in adrenal mitochondria, where it is involved in the synthesis of steroid hormones. Malfunctioning of such processes underlies several pathological conditions.

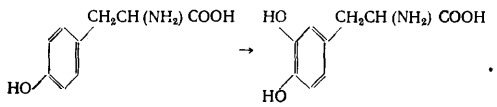
Several micro-organisms hydroxylate hydrocarbons, using them as nutrients[3,5-7,23,24]. This ability has been examined during recent years with the aim of producing foodstuffs and fodder from petroleum hydrocarbons and natural gas[23,24]. The American Mobil Oil Company in 1967 patented the enzymic oxidation of all classes of hydrocarbons[6]. The universal character of the oxidation is explained by the use of various strains of four species of micro-organisms—*Pseudomonas*, *Nocardia*, *Bacillus*, and *Mycobacterium*.

Hydroxylation of foreign compounds can be accomplished not only in the endoplasmic reticulum of liver cells but also in the lungs, gastrointestinal tract, skin, and kidneys[25-27]. The endoplasmic reticulum is a system of membranes ~80 Å thick located in the cytoplasm. On differential centrifugation, fragments of these membranes form the so called microsomal fraction remaining in the supernatant liquid after the separation of heavy particles—nuclei and mitochondria.

Complicated hydroxylating systems, wherever they are found—in mammalian liver microsomes, in adrenal mitochondria, or in bacteria— are in all cases multicomponent in character. Table 1 lists the most important mono-oxygenases studied during recent years.

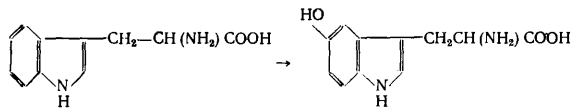
The review by Maslova et al.[4] has discussed in detail aspects of the physiological role of the mono-oxygenases of liver microsomes, induction of the synthesis of the microsomal hydroxylating system, and its hormonal regulation. We would like to consider only the part played by mono-oxygenases in the physiological state of the brain. During recent years great advances have been made in investigating enzymes of the central nervous system, especially those affecting metabolism of the biogenetic amines involved in the specific functions of nerve cells. Such amines include tyramine, dopamine, adrenaline, noradrenaline, serotonine, etc. Their biosynthesis and catabolism are regulated by the activity of enzyme systems, in particular mono-oxygenases, and govern the normal physiological state of the brain[63]. In the nerve endings and in certain compartments of the cerebrum tyrosine

hydroxylase catalyses the hydroxylation of tyrosine to 3',4'-dihydroxyphenylalanine[64]:



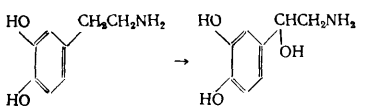
The purified enzyme was obtained from the medullary layer of bovine adrenal glands[64]. The search for multiple forms of tyrosine hydroxylase is continuing. This enzyme is active under aerobic conditions in the presence of tetrahydrofolic acid or 2-amino-5,6,7,8-tetrahydro--4-hydroxy-6,7-dimethylpteridine and of Fe^{2+} and K^+ ions[65]. It is inhibited *in vitro* by amino-acids and their derivatives, in particular by noradrenaline, catechols, and indoles. Normally it hydroxylates only tyrosine. In Parkinson's disease the hydroxylation is assumed to be possible of dihydroxyphenylethylamine, whose injection into animals causes "chemical sympathectomy", i.e. cessation of the functions of the nerve cells mediated by pulses of noradrenaline, and also complete inhibition of the activity of tyrosine hydroxylase[66].

Tryptophan hydroxylase, which catalyses the hydroxylation of tryptophan to 5'-hydroxytryptophan



has been detected in brain[67-70], especially in the stem[71]. The purified enzyme has been obtained from bovine brain[71]. The presence of 2-amino-5,6,7,8-tetrahydro-4-hydroxy--6,7-dimethylpteridine is necessary for functioning of the enzyme. In contrast to the liver enzyme, brain tryptophan hydroxylase hydroxylates only *L*-tryptophan at position 5. The hydroxylation of tryptophan limits the rate of biosynthesis of serotonine in the brain[72].

Dopamine β-hydroxylase, which catalyses the hydroxylation of dopamine to noradrenaline



was identified as early as 1964. It catalyses the concluding stage in the biosynthesis of noradrenaline, which mediates the nervous impulses in the synapses of the sympathetic nervous system. The development of certain forms of psychic depression is attributed to an insufficiency of adrenaline. Many psychotropic agents change the noradrenaline content of the brain. Accumulation of excess of noradrenaline in a cell inhibits further hydroxylation of dopamine.

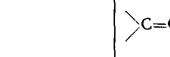
III. TYPES OF REACTIONS CATALYSED BY MONO-OXYGENASES

The reactions catalysed by mono-oxygenases are extremely diverse (Table 2). Liver microsomes are able to metabolise substances of various structures, i.e. to effect various reactions, among which the most common is the hydroxylation of aliphatic compounds. In practice this is the most important reaction in the microbiological transformation of steroidal compounds[8,9]. Steroid hydroxylases of micro-organisms are known for almost all positions in the steroid system—ring system, side-chain, angular methyl groups—but all the hydroxylations studied in the steroid series occurred at a saturated carbon atom. Steroid hydroxylases are met not only in micro-organisms but also, as already noted, in animal tissues[78-80]. Fermentation by micro-organisms usually introduces one oxygen atom—more rarely two atoms—into the steroid molecule. Liver microsomes oxidise the terminal groups of aliphatic hydrocarbons to primary alcohols[53] and effect the ω-hydroxylation of aliphatic acids to ω-hydroxy-acids[53,81-84]:

$$CH_3(CH_2)_nCOOH \rightarrow HOCH_2(CH_2)_nCOOH.$$

The second most common reaction catalysed by mono-oxygenases is the hydroxylation of aromatic systems[47,48,55,56,60,85] with the formation of phenols. This reaction plays an important part in the metabolism of aromatic amino-acids. The position of the entering hydroxy-group is often determined by the presence of functional substituents in the aromatic ring.

Table 2. Reactions catalysed by mono-oxygenase enzymes.

Type of reaction	Reaction	Ref.
1. Hydroxylation of aliphatic compounds		12, 14, 30–40, 73, 74
2. Hydroxylation of aromatic compounds	$ArH \rightarrow ArOH$	47, 48, 55, 56, 60, 64, 67–70
3. Epoxidation		8, 9, 75
4. Formation of lactones		76
5. Deamination		4
6. Oxidative *N*-, *O*-, and *S*-dealkylation	$C_6H_5OCH_3 \rightarrow C_6H_5OH + CH_2O$ 	14
7. *N*-Hydroxylation and *N*-oxidation		77
8. Formation of sulphoxides		12

Epoxidation occurs in microbiological transformations of unsaturated steroids[8,9]. Enzymic formation of α-oxides has now been described from Δ^5-, $\Delta^{9(11)}$-, Δ^{11}-, and Δ^{14}-steroids. The epoxidation and the hydroxylation of steroids are very often accomplished by the same enzyme system[8]. Fat-soluble amines are deaminated in the presence of mono-oxygenases, being converted into ketones and ammonia. Amphetamine and its analogues undergo this reaction in the animal liver. Mono-oxygenases catalyse also *N*-, *O*-, and *S*-dealkylation, hydroxylate at a nitrogen atom, and oxidise substrates at nitrogen and sulphur atoms.

With all their variety the reactions of mono-oxygenases have an important common feature: only one oxygen atom is transferred to the substrate by the reaction.

IV. COMPOSITION AND PROPERTIES OF MONO-OXYGENASE ENZYME SYSTEMS

Hydroxylating enzyme systems are complicated multicomponent protein structures. All mono-oxygenases can be divided into two large groups: the first group includes *enzymes containing no metal ion or complex*; the second group comprises *enzymes containing one or more metal atoms*, which are therefore metal proteins.

Examples of this first group of enzymes are imidazolyl acetate mono-oxygenase [14] (the electron donor for which is NADH, while the prosthetic group contains flavin adenine dinucleotide (FAD) and is a flavoprotein), kynurenine 3-mono-oxygenase [41,42,86,87], salicylate hydroxylase [73], *p*-hydroxybenzoate hydroxylase [74], and *L*-lysine mono-oxygenase [88]. The prosthetic groups of these enzymes are usually FAD-containing proteins [89-93]. The kinetics and the mechanism of the action of enzymes of this group will be discussed in detail in Section V.

Enzymes of the second group, which contain a metal ion, are more numerous and have been more thoroughly studied. Among them is tyrosinase, a copper protein, the cosubstrate being an *O*-dihydroxyphenol reaction product [94]. Dopamine β-mono-oxygenase contains two copper atoms per enzyme molecule [95]. Phenylalanine hydroxylase, containing 1–2 iron atoms per enzyme molecule, has now been well studied [96-100]; the enzyme isolated from rat liver exists in two forms separable by electrophoresis, each of which may be either a monomer, a dimer, or a tetramer (with respective molecular weights 51 000–55 000, 110 000, and 210 000). The dimers dissociate into the monomeric form when the enzyme is diluted and the temperature is raised from 0 to 30°C.[96] The stoichiometry of the reaction of phenylalanine hydroxylase can be expressed

Tetrahydropterin + Phenylalanine + O_2 → Quinonoid dehydropterin + Tyrosine + H_2O.

Tetrahydropterin is the cosubstrate undergoing dehydrogenation. The iron atom is present in the enzyme in the high-spin form of Fe^{3+}. The hydroxylase is inhibited by loss of the iron atom or on addition of a compound which chelates the metal. The electron spin resonance spectrum of purified phenylalanine hydroxylase is characterised by a signal with $g = 4.23$, which is due to the high-spin form of the iron ion. Addition of a substrate to the enzyme leads to disappearance of this signal, which indicates that the iron has been reduced to Fe^{2+}. [98] The enzyme inactivated by removal of iron is reactivated by the addition of iron(II) chloride. The study of phenylalanine hydroxylase isolated from human liver by autopsy has begun quite recently [99,100]. Two forms of the enzyme—dissolved at 6000 *g* and precipitated at the same acceleration—are obtained [100]. Much in common is found between the properties of the enzymes isolated from human and rat livers. The Michaelis constant K_m varies with pH and the 2-amino-5,6,7,8-tetrahydro-4-hydroxy-6,7-dimethylpteridine concentration; at the optimum pH it is 5×10^{-4} M. [100]

Enzymes containing as prosthetic group the so called cytochrome P-450 form the largest group studied intensely during recent years. These enzymes can in turn be divided into three subgroups depending on their occurrence in Nature—mono-oxygenases in microsomes of the mammalian liver [102-112], in mitochondria of the adrenal glands, and of bacterial origin [60-62, 89-93, 118, 119]—between whose enzyme systems exist substantial differences, although they all usually contain cytochrome P-450. Scheme 1 shows for comparison the electron-transfer chains established in the three subgroups of enzymes [4].

Scheme 1

liver microsomes

NADPH → flavoprotein II → non-haemin Fe protein → cytochrome P-450 → O_2
↓
cytochrome c

adrenal mitochondria

NADPH → flavoprotein III → non-haemin Fe protein → cytochrome P-450 → O_2
(adrenodoxin)

bacterial mono-oxygenases

Methylene hydroxylase
NADPH → flavoprotein → putidaredoxin → cytochrome P-450 → O_2
ω-Hydroxylase
NADPH → flavoprotein → rubredoxin → unidentified cytochrome → O_2

Scheme 1 shows that the electron (hydrogen) donor is NADPH, or NADH in the case of bacterial mono-oxygenases. Hydrogen is transferred from the donor to the flavin group of the protein reductase together with an electron pair by a mechanism of hydride migration. The protein reductase is equally capable of two- and one-electron transfers. The next link in the chain of electron transfer is a protein generally containing iron and sulphur atoms, termed a non-haemin iron protein adrenodoxin with mitochondrial, putidaredoxin with methylene hydroxylase, and rubredoxin in alkane carboxylic acid systems. The role of the iron protein may be different in different cases: although its presence is not necessary in the last system, it is highly specific with methylene hydroxylase and cannot be replaced by any other protein. Putidaredoxin and adrenodoxin play a very direct part in the transfer of electrons along the chain, and we shall discuss them in greater detail later. There is as yet no direct indication of the participation of non-haemin iron in electron transfer in microsomes, although it is supposed to act as a component between flavin and cytochrome P-450.

The terminal electron carrier in microsomal, mitochondrial, and bacterial chains is cytochrome P-450, which has now been isolated from liver microsomes [101-105], adrenal mitochondria [113-116], and bacteria [118,119]. It is a haem protein, which in the reduced state forms with a molecule of carbon monoxide a stable complex having an absorption maximum at 450 nm. The cytochrome is oxidised fairly readily by molecular oxygen, and can be reduced again with NADPH or dithionite. It contains not only iron but also copper. Treatment with proteases, amides, ketones, phenols, and anilines converts the cytochrome into a form possessing no enzymic activity, with the Soret band of the carbonyl complex at 420 nm, which is characteristic of other cytochromes. The spectrum of the oxidised form of cytochrome P-450 contains absorption maxima at 360, 416, 535, 570, and 650 nm. The enzyme from liver microsomes contains a mixture of low-spin and high-spin forms of iron. The spectrum of the reduced enzyme is distinguished by a low absorption coefficient and displacement of the Soret band to shorter wavelengths with maxima at 412 and 557 nm. In the oxidised state, cytochrome P-450 from liver microsomes gives an e.s.r. signal with components g_x, g_y, and g_z of the *g*-factor of 1.91, 2.25, and 2.41 respectively. This signal characterises a low-spin state of tervalent iron in an asymmetric environment. The low-spin form of the cytochrome passes into a high-spin form with an anisotropic e.s.r. signal either at low pH or on treatment with thiol inhibitors. The cytochrome from liver microsomes contains a lipid component, which confers on it the ability to combine with hydrophobic compounds. It has recently been shown [120] that reduced cytochrome P-450 from microsomes forms with molecular oxygen a complex having an absorption maximum at 440 nm, twenty times as rapidly

as the carbonyl derivative: the rate constants for the interaction of cytochrome P-450 with molecular oxygen and with carbon monoxide at 25°C are respectively 4.4×10^6 and 2.4×10^5 M^{-1} s^{-1}. Cytochrome P-450 isolated from the mitochondria of adrenal glands differs little from liver samples. Specimens from the two sources have analogous optical and e.s.r. spectra [114].

The cytochrome isolated from camphor-oxidising microorganisms is now the most thoroughly studied [118,119,121]. Its optical and e.s.r. spectra have been well investigated, as well as its Mössbauer spectra, for which the natural cytochrome was enriched with the iron-57 isotope. In the presence of the substrate (camphor) the oxidised cytochrome consists of a mixture of high-spin ($S = 5/2$) and low-spin ($\frac{1}{2}$) haem iron Fe^{3+}. Removal of camphor converts the former into the latter form of iron. Anaerobic reduction of cytochrome P-450 gives the high-spin form of Fe^{2+} ($S = 2$), no paramagnetic effects being observed even in a strong field. The Mössbauer spectra of cytochrome $P\text{-}450_{camph}$ are analogous to those of oxygenated haemoglobin. Cytochrome $P\text{-}450_{camph}$ is a protein of molecular weight 45 000 consisting of a polypeptide chain and iron protoporphyrin IX. Axial coordination of haem P-450 still remains an open question: it is assumed merely that cysteine sulphur and histidine nitrogen are axial ligands. The reduced enzyme gives a complex with molecular oxygen, which has been observed by optical methods [118,121]: a new spectral band appears with maxima at 555, 418, and 355 nm. [118] This is accompanied by disappearance of the e.s.r. signal having $g = 2.26$, characteristic of the low-spin Fe^{3+} form. The complex cytochrome $P\text{-}450_{camph} \rightarrow O_2$ is fairly stable at low temperatures (4–8°C), but is slowly converted into the high-spin form of Fe^{3+} on standing. Thus the haem nature of P-450 cytochromes has now been firmly established, as has their direct participation in the hydroxylation of various substrates. Formation of an oxygenated derivative of the cytochromes on enzymic hydroxylation has been proved.

Cytochrome P-450 is preceded in the electron-transfer chain by so called iron- and sulphur-containing proteins, which are distinguished from other iron-containing proteins by the fact that the metal is not attached to complexing organic ligands [122]. In rubredoxin a single iron atom is coordinated with four cysteine sulphur atoms. The biological role of rubredoxin is not always clear: it consists mostly in electron transfer. In steroid-hydroxylating systems this protein is termed adrenodoxin. It has been isolated in a free form [117] and has been well characterised. Adrenodoxin contains 2 g-atoms of iron and 2 moles of labile sulphur per mole of protein; its molecular weight is 12 500 and its simple polypeptide chain contains 114 amino-acids. The structure of the active centre is dinuclear–tetrahedral. The most recent value [114] for the redox potential of adrenodoxin is −0.27 V at pH 7.0. Adrenodoxin can be completely reduced by dithionite, NADPH, or adrenodoxin reductase.

A protein named putidaredoxin, which contains both iron and sulphur, plays an especially important part in the hydroxylation of camphor: it ensures transfer of a second electron to the ternary complex of cytochrome with the substrate and oxygen [119]. Putidaredoxin is very specific, and cannot be replaced by another sulphur-containing protein, e.g. adrenodoxin, a component of steroid 11 β-hydroxylase. Yet NADH dehydrogenase can be replaced by a different dehydrogenase, in the electron-transfer chain of the camphor-hydroxylating system, without loss of enzymic activity. Physicochemical investigation of putidaredoxin (by magnetic susceptibility, electron spin resonance, electron–nuclear double resonance, Mössbauer spectra, and circular dichroism spectra) indicates the presence of two iron atoms in the oxidised form in a high-spin state ($S = 5/2$). Thus it has been established that in several cases a non-haemin protein takes part in the transfer of electrons during the hydroxylation of a substrate, although its presence is not necessary in a paraffin-acidifying system.

Non-haemin proteins are preceded in the electron-transfer chain by protein reductases, usually flavoproteins capable of transferring two electrons. The reductase isolated from a system effecting the enzymic ω-oxidation of aliphatic acids contains FAD as prosthetic group (1 mole $mole^{-1}$ protein) and has molecular weight 55 000. [84] The reductase is very specific, interacting with rubredoxin to give a complex of dissociation constant 2.1×10^{-7} M. The activation energy of the enzyme-catalysed reduction of rubredoxin by NADH is 5.4 kcal $mole^{-1}$.

Thus hydroxylating enzyme systems are composite multicomponent protein structures. Every component effects the transfer of electrons. Many obscurities and mysteries still remain in the structure and properties of individual parts of enzyme systems.

V. KINETICS AND MECHANISM OF THE ACTION OF MONO-OXYGENASES

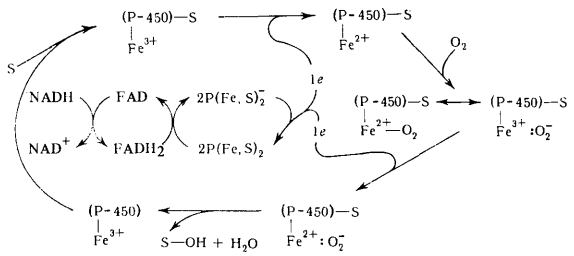
Kinetic study of the reactions of mono-oxygenases and measurement of the rates of individual stages in the composite enzymic process will provide valuable information on the mechanism of the action of these enzymes. It must be remembered, however, that study of the mechanism on extracts and even on purified preparations almost always yields only tentative conclusions on the mechanism of the oxidising stage.

Quantitative data have now been obtained for various stages in the oxidation of camphor in the presence of methylene hydroxylase [118,121,123,124]. Cytochrome P-450 reacts at very high rates with molecular oxygen to give a complex. The rate constant of formation of the camphor complex of this enzyme is 3.7×10^6 M^{-1} s^{-1} at 8°C [123], and the equilibrium constant of the complex is 0.47×10^6 M^{-1}. The enzyme–substrate complex itself has been isolated in the crystalline state [124]. It has been firmly established that oxidised cytochrome adds camphor, after which it acquires an electron. The enzyme–substrate complex then adds oxygen to form an enzyme–substrate–O_2 ternary complex, which acquires a second electron to form oxidised camphor and oxidised cytochrome. The rate of addition of camphor and oxygen to the enzyme exceeds hundredfold the rate of formation of the product. From the kinetic measurements and analysis of the functions of the component parts Scheme 2 has been suggested for the action of the methylene-hydroxylating system (S is the substrate, and S–OH the oxidised substrate). A distinguishing feature of Scheme 2 [121] is that both electrons for the reduction of oxygen are supplied by putidaredoxin.

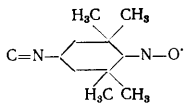
Study of the redox cycle of cytochrome P-450 from liver microsomes has shown that it involves formation of an oxygenated intermediate of the reduced cytochrome. This intermediate was detected by differential spectrophotometry, and the kinetics of its appearance has been studied. The rate constant of the reaction between cytochrome and oxygen has recently been measured, by stopped-flow flash photolysis, as 4.4×10^6 M^{-1} s^{-1} at 25°C. [120] Scheme 3 shows the course of electron transfer

in liver microsomes during hydroxylation of the substrate[103]. Here the electron donor for the oxygenated form of reduced cytochrome P-450 is cytochrome b_5.

Scheme 2

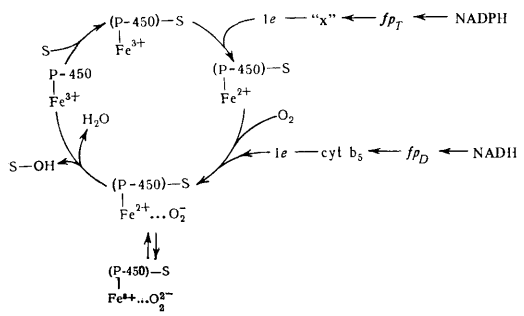


The spin-label method[110-112] has recently been used to study the molecular structure and the mechanism of the action of cytochrome P-450. The enzyme from liver microsomes interacted with the isocyanide spin-label



with the appearance of absorption bands around 435 and 455 nm characteristic of isocyanide derivatives of cytochrome. The e.s.r. spectra of liver microsomes treated with the spin-label suggest considerable retardation of the molecular motion of the latter, caused by its hydrophobic environment. The frequency of molecular rotation of the label increases on addition of the substrate to be hydroxylated (hexobarbital). The form of the e.s.r. spectra of the label indicates that the haem molecules to which it is attached are far apart and do not form dimeric structures. The active centre of cytochrome P-450 is assumed to be a haem group surrounded by non-polar amino-acid residues, whose spatial arrangement relative to the haem changes in definite fashion on interaction of the cytochrome with substrates.

Scheme 3



Considering now the mechanism of the action of metal-free mono-oxygenases, we note that the stopped-flow technique has been used to elucidate certain aspects of the reaction mechanism of salicylic hydroxylase from *Pseudomonas putida*[92]. With pH 7.0 at 25°C the rate constant of attachment of the enzyme to the substrate is 1.8×10^7 M^{-1} s^{-1}, while that of the reverse reaction is 62 s^{-1}. Denoting the enzyme, flavin, and substrate as E, F, and S respectively, we can write the reaction

$$EF{-}S + NADH + H^+ \rightarrow X_1 \xrightarrow{k=230\ s^{-1}} EFH_2{-}S + NAD^+$$
$$EFH_2{-}S + O_2 \rightarrow X_2 \xrightarrow{k=21\ s^{-1}} EF + \text{catechol} + CO_2 + H_2O$$

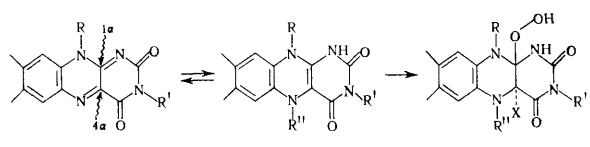
in which EF–S and EFH_2–S are the oxidised and the reduced complexes respectively, while X_1 and X_2 are kinetically active species. The rate of reduction of flavin in the presence of salicylate exceeds the rate in its absence by a factor exceeding 2000. The limiting stage of the whole process is oxidation of the reduced complex by an oxygen molecule.

Use of the stopped-flow method to study the kinetics of the formation of the enzyme–substrate complex of *p*-hydroxybenzoic hydroxylase shows[89] that the rate of complex formation is very high, and the reaction itself takes place in two stages

$$EF + S \underset{k_2}{\overset{k_1}{\rightleftarrows}} EF \sim S \underset{k_4}{\overset{k_3}{\rightleftarrows}} EF{-}S$$

the first of which is far more rapid than the second (k_3 = 480 s^{-1} and k_4 = 140 s^{-1}). The multistage character may be due to isomerisation of the enzyme–substrate complex or to conformational changes in the enzyme. Examples of the multistage formation of complexes with substrates are known also for enzymes of other classes[125-128]. Thus multistage interaction of enzyme with substrate has been found in ribonuclease–cytidine 3-phosphate, chymotrypsin–proflavin, lysozyme–oligosaccharide, etc. systems. The reaction of *p*-hydroxybenzoic hydroxylase from the microorganism *Pseudomonas fluorescens* with a 2,4-dihydroxybenzoate in the presence of NADH and molecular oxygen has now been studied in stages. The anaerobic reduction of the complex of *p*-hydroxybenzoic hydroxylase with the 2,4-dihydroxybenzoate by NADH has been studied spectrophotometrically by the stopped-flow technique, and formation of at least three intermediate compounds has been shown during the process. All three intermediates absorb in the long-wavelength region, and exhibit no e.s.r. signals. Oxidation of the reduced enzyme–substrate complex by oxygen has also been studied, and an intermediate—an oxygenated form of the flavin prosthetic group attached to the enzyme—has been clearly recorded. The second intermediate was identified as an oxidised "enzyme–product" complex; it undergoes conversion at a rate close to the maximum rate of an enzymic process. The suggested[90] oxygenated intermediate of flavins has been detected quite recently when completely reduced flavin and the flavoprotein interact with singlet molecular oxygen[129]. The structure of the oxygenated flavin was established from the absorption spectra and by means of a high-resolution mass spectrometer fitted with a computer. The oxygenated form is characterised by absorption at 500–680 nm and a peak at 375 nm.

Scheme 4

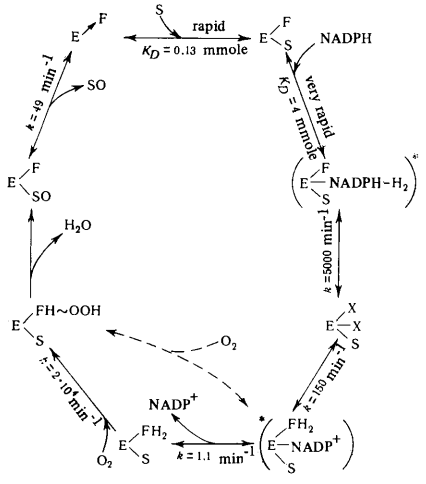


where X = $-OCH_3$; $-SCH_2CH(NH_2)COOCH_3$

Scheme 4 represents the formation of oxygenated flavin with oxygen in its first excited state ($^1\Delta g$). Oxygen attacks position 1α, with formation of a hydroperoxy-derivative of flavin. The mechanism depicted in Scheme 5 was suggested[90,91] on the basis of kinetic investigations for the interaction of *p*-hydroxybenzoic hydroxylase with the 2,4-hydroxybenzoate substrate, F being flavin attached to the enzyme E, the X unidentified species, and SO 2,3,4-trihydroxybenzoate, while the asterisk denotes charge-transfer complexes. Scheme 5 shows that the slowest

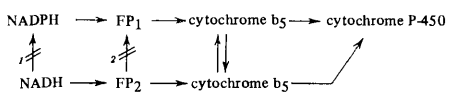
stage in the reaction is charge transfer in the enzyme–substrate–NADP complex ($k = 1.1$ min^{-1}). The other stages occur much more rapidly. Formation of an oxygenated flavin derivative in the enzyme–substrate complex precedes transfer of an oxygen atom to the substrate.

Scheme 5



Investigation of the prestationary and steady-state kinetics of the reactions of mono-oxygenase enzymes provides indications of the limiting stage in the overall enzymic process and of the intermediate complexes responsible for activating molecular oxygen. Experience shows that hydrophobic interaction of the substrate with hydrophobic (e.g. lipid) portions of the enzyme molecules alone is insufficient for the enzymic reaction to occur[109–111]: the inert oxygen molecule must be activated during the reaction. This main function of mono-oxygenases is accomplished by cytochrome P-450, which forms an oxygenated intermediate compound with molecular oxygen, and by the flavin groups of mono-oxygenases free from metal ions, which form with molecular oxygen a 1α-hydroperoxy-derivative of flavin, as has definitely been proved quite recently. Thus the oxygen molecule is activated by two-electron reduction either by an iron ion or by flavin reduced in the electron-transfer chain. The two-electron reduction of oxygen involving cytochrome P-450 in Scheme 3 contains many obscurities connected with the source of the second electron for reduction, since the interaction of NADPH and NADH-specific electron-transfer chains is still not clear[130]. Recently exchange of equivalents undergoing reduction, between NADPH and NADH-specific electron-transfer chains, has been discussed[131]. In Scheme 6 this exchange occurs with the aid of cytochrome b_5. Exchanges *1* and *2* do not take place.

Scheme 6



In spite of great achievements in the kinetic study of enzymic reactions of mono-oxygenases and their individual stages, the central problem—the mechanism of the activation of oxygen—cannot yet be regarded as solved, since the structure of the active oxygen in cytochrome P-450 is completely unknown. It is clear only that transfer of an oxygen atom to the substrate is not always the limiting stage. Since direct examination of the transition state is impossible with most enzymic reactions, it becomes necessary to study model systems and model reactions reflecting individual aspects of the complicated enzymic process. Only model reactions and model systems will enable details of the activation of molecular oxygen to be elucidated.

Three methods—theoretical considerations, investigation of the properties of enzymes, and study of the mechanisms of chemical reactions and their catalysis—are available for solving the problem of establishing the mechanism of enzymic action[132]. According to Jencks, "... to understand the mechanism of catalysis of an enzymatic reaction one would first like to understand the mechanism of the non-enzymatic reaction and the means by which this reaction can be accelerated". In Section VI we shall discuss in detail problems involved in modelling the action of mono-oxygenase enzymes.

VI. METHODS OF SIMULATING MONO-OXYGENASE ENZYMES

With all the complexity of enzymes, they obey the same thermodynamic and kinetic laws as do ordinary catalysts, so that even simple catalysts simulate in some measure certain aspects of the action of enzymes. Concerning the modelling of enzymes it is Shilov's opinion that "this concept can most usefully be applied in the light of the purpose of the investigation rather than on the basis of the degree of similarity between the catalyst studied and the enzyme which this catalyst simulates". Many reviews have been published[132–138] on the simulation of enzymes. A combined approach may yield significant results, as occurred for the enzymic fixation of molecular nitrogen[137]. By learning from Nature and using chemical concepts, we can discover novel, sometimes surprising reactions.

The action of a mono-oxygenase transfers one atom of an oxygen molecule to a substrate molecule. It is therefore most advisable to study firstly ways in which oxygen is transferred to a substrate by various systems and their mechanisms. The investigation of mono-oxygenases has shown that an oxygen atom can be incorporated into a substrate only after the oxygen molecule has acquired two electrons. All systems which transfer oxygen to a substrate can be divided into two broad groups: the first group includes metal ions and complexes, whose oxidation provides two electrons for the oxygen; the second group comprises compounds of peroxide character, in which oxygen has already been activated, since it possesses these two electrons. In the former case oxidation of the substrate involves that of the metal ion or complex. In the latter case an oxygen atom is transferred directly to the substrate from the peroxy- or hydroperoxy-compound. Imitation of enzymic oxygen transfer will be more complete the wider the range of reactions which can be accomplished by the suggested model for mono-oxygenase (Table 3). *N*-Oxides, ozone, and oxo-anions of metal salts are also able to transfer oxygen to a substrate.

Henceforward we shall discuss in detail the reactions of each group of suggested model systems and the mechanism of their action. The most interesting are the first group of systems, containing a metal ion or complex together with molecular oxygen. Table 3 lists several such systems (with aromatic substrates the proportions of isomeric phenols formed are given in the sequence—*ortho* : *meta* : *para*).

Table 3. Systems containing a metal ion or complex and molecular oxygen.

System	Substrate	Products	Ref.
Fe^{2+} + ascorbate	dehydroepiandrosterone	7-hydroxyandrostenones	139
Fe^{2+} + ascorbate	cortexolone	cortisol + cortisone	140,141
Fe^{2+} + ascorbate + EDTA	anisole	methoxyphenols 43:18:39	142
Fe^{2+} + 2,4,5-triamino-6-hydroxypyrimidine	anisole	methoxyphenols 49:13:38	143
Fe^{2+} + thiosalicylic acid	acetanilide	phenols 57:3:40	144
Fe^{2+} + thiosalicylic acid	toluene	cresols 61:13:16	144
Fe^{2+} + thiosalicylic acid	napthalene	1-naphthol 11% 2-naphthol 9%	144
Fe^{2+} + *N*-benzyl-1,4-dihydronicotinamide	arene	hydroxyarene	145
Fe^{2+} + tetrahydropterin	phenylalanine	tyrosine 2:1:1	146
Fe^{2+} + tetrahydropterin	tryptophan	5-hydroxytryptophan + melanin + kynurenine	146,147
Haemin + thiosalicylic acid	cyclohexane	cyclohexanol	148
Fe^{2+} + EDTA	toluene	cresols 38:24:38	145
Fe^{2+} + EDTA	anisole	methoxyphenols 56:8:36	145
Fe^{2+} + EDTA	fluorobenzene	fluorophenols 2:45:53	145
$FeCl_2$ (acetone or methanol)	cyclohexane	cyclohexanol	149
$TiCl_3$	acetanilide	phenols 35:32:33	150
$TiCl_3$	toluene	cresols 61:16:23	145
$TiCl_3$	anisole	methoxyphenols 54:0:46	145
$TiCl_3$	fluorobenzene	fluorophenols 2:33:65	145
$TiCl_3$	nitrobenzene	nitrophenols 4:36:60	145
$TiCl_3$	cyclohexane	cyclohexanol + cyclohexanone	151
CuCl	toluene	cresols 29:29:49	145
CuCl	anisole	methoxyphenols 75:8:17	145
CuCl	fluorobenzene	fluorophenols 30:68:2	145
$SnHPO_4$	toluene	cresols 46:38:16	145
$SnHPO_4$	anisole	methoxyphenols 53:20:17	145
$SnHPO_4$–organic solvent	acetanilide	phenols 34:44:22	152
$SnCl_2$–acetonitrile	alkanes	isomeric alcohols	153
$SnCl_2$–acetone	cyclohexane	cyclohexanol	154
$MoCl_3$	cyclohexane	cyclohexanol	151
$Mo(CO)_6$–acetonitrile	naphthalene	1-naphthol	155
$Mo(CO)_6$–acetonitrile	benzene	phenol	156
$MoO(S_2CNR_2)_2$	triphenylphosphine	triphenylphosphine oxide	157

Table 4 sets out the reactions of peroxy-acids and of several peroxy-compounds [158–173] with a series of substrates, to which oxygen is transferred on the pattern of the action of mono-oxygenases containing flavoproteins but no metal ion or complex. Reactions of peroxy-acids with alkenes are omitted from Table 4, for their mechanism and kinetics have been thoroughly studied [174]. Aromatic substrates are treated as in Table 3.

Table 4. Reactions of peroxy-acids and peroxide compounds.

Reagent	Substrate	Products and constants	Ref.
CF_3CO_3H	benzene	phenol	158
CF_3CO_3H	phenol ethers	phenoxyphenols	159
CF_3CO_3H	anisole	methoxyphenols, quinones	160
CF_3CO_3H	anisole	methoxyphenols 73:0:27	161
CF_3CO_3H	toluene	cresols 78:2:20	161
CF_3CO_3H	fluorobenzene	fluorophenols 17:0:83	161
CF_3CO_3H	acetanilide	phenols 43:1:56	56
CF_3CO_3H	*p*-deuterotoluene	*p*-methylphenol 2-deutero-4-methylphenol	162
CF_3CO_3H	naphthalene	$K = 1.6 \times 10^8 \exp(-14400/RT)$	163
CF_3CO_3H	2-methylbutane	isomeric butanols	15
CF_3CO_3H	methylcyclohexane	isomeric methylcyclohexanols	15
CH_3CO_3H	*p*-methylphenols	muconic acids and lactones	164
CH_3CO_3H	hexamethylbenzene		165
CH_3CO_3H, HCO_3H	phenol	catechol-quinol	166
CH_3CO_3H	naphthalene	$K = 6.2 \times 10^9 \exp(-21000/RT)$	167
CH_3CO_3H	anisole	$K = 6.3 \times 10^8 \exp(-17000/RT)$	167
CH_3CO_3H	phenol	quinones + muconic acid	168
CH_3CO_3H	1-methoxynaphthalene	muconic acids	169
CH_3CO_3H	*p*-methylphenol	*cis, trans*-β-methylmuconic acid	170
m-Chloroperbenzoic acid	4-methyl-2,6-di-t-butylphenol		108
Autoxidising dihydroalloxazines			171
$MoO(O_2)_2L_1L_2$*	allyl alcohol	glycidol	172
$MoO(O_2)_2L_1$	allyl alcohol	glycidol	172
$MoO(O_2)_2L_1$	naphthalene	1-naphthol + quinones	173

*L_1 = Hexametapol; $L_2 = H_2O$.

Model systems of the first type (Table 3) can in turn be divided into two subgroups: the first subgroup—tin(II) hydrogen orthophosphate, tin(II) and molybdenum(III) chlorides, and hexacarbonylmolybdenum—contains a metal ion capable of transferring not one but two or more electrons; the second subgroup includes a metal ion capable of one-electron transfer and a redox-active ligand—ascorbic acid, thiosalicylic acid, tetrahydropterin, and pyrimidines. Table 3 shows that model systems of the first type effect the hydroxylation of aliphatic [139–141, 151, 154] and aromatic [142–147, 155, 156] compounds, and also oxidise triphenylphosphine to its oxide [157]. Furthermore, systems containing an Fe^{2+} ion and a redox-active ligand can convert alkenes into epoxides [138]. Thus model systems of the first type accomplish many of the reactions catalysed by mono-oxygenases (Table 2). The most important task is to recognise the species containing active oxygen and capable of accomplishing all the reactions enumerated in Table 3. The radicals HO· and HO_2· are possible active species, but these free radicals cannot be the activated forms of oxygen in enzyme systems, since they would destroy the cell. They can be stabilised by metal ions: HO_2· is converted into FeO_2^{2+} (complex III) on interaction with Fe^{3+}, but HO· forms FeO^{2+} (complex II). In such a stabilised state the radicals HO· and HO_2· may be oxygen carriers in biological oxidation. An important characteristic of a species attacking an aromatic substrate is the distribution of isomers and the orienting influence of the substituent in the benzene ring. For all the cases listed in Table 3 the distribution of isomeric phenols differs significantly from that typical of HO· radicals generated by various methods—with Fenton's reagent,

radiolytically, etc.[2]—which means that these radicals are not the active intermediate for all the systems investigated. Several workers have suggested that the radical $HO_2^{\cdot}$ may act as attacking species for the $TiCl_3 + O_2$ and $Sn^{2+} + O_2$ systems[152]. The distribution of isomeric phenols indicates that the substrate is attacked by a less electrophilic species than HO· ; yet it is well known that $HO_2^{\cdot}$ is more electrophilic than HO· (with electron affinities respectively of 3.04 and 2.65 eV—Ref. 1, p. 207). Thus either the radical $HO_2^{\cdot}$ is unable to function as the active species or it does so in a less electrophilic state than that of HO· , as a consequence of interaction with the solvent (hydrogen bonding). It is noteworthy also that $HO_2^{\cdot}$ may be less active towards aliphatic and aromatic substrates than is HO· .[2,175] The hydroxylating ability of the former radical towards aromatic compounds has been convincingly proved by one of the Reviewers[2], yet the activity of HO· towards indigodisulphonate exceeds that of $HO_2^{\cdot}$ by factors of 10^6.[175]

Study of the $Sn^{2+} + O_2$ system is of great value in the choice between the radical $HO_2^{\cdot}$ and other attacking species. It is well known that the Sn^{2+} ion can be oxidised either successively through Sn^{3+} or directly to Sn^{4+} with simultaneous loss of two electrons[176]. In the two-electron oxidation oxygen is transferred to the substrate according to the equations

$$Sn^{2+} + O_2 \rightleftarrows [Sn^{2+}O_2]$$
$$[Sn^{2+}O_2] + S \rightarrow Sn^{4+}O + SO$$

a simple scheme suggested by Ullrich[152]. It has been proved, however, that in aqueous solution oxidation of the Sn^{2+} ion by molecular oxygen has a radical-chain mechanism[176,177]:

$$Sn^{2+} + O_2 \xrightarrow{H^+} Sn^{3+} + HO_2^{\cdot}$$
$$Sn^{2+} + O_2 \xrightarrow{H^+} Sn^{4+} + HO_2^{\cdot}$$
$$Sn^{2+} + HO_2^{\cdot} \xrightarrow{H^+} Sn^{3+} + H_2O_2$$
$$Sn^{2+} + H_2O \xrightarrow{2H^+} Sn^{4+} + 2H_2O$$
$$Sn^{3+} + Sn^{3+} \rightarrow Sn^{2+} + Sn^{4+} .$$

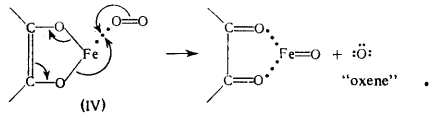
The retarding effect of inhibitors—4-methyl-3,6-di-*p*-tolyliminocyclohexa-1,4-dienylamine, potassium trioxalatocobaltate, etc.—confirms the radical-chain mechanism of the oxidation of tin(II) in aqeuous solution[176]. Thus in aqueous solutions or in aqueous-alcohol and aqueous-acetone mixtures the hydroxylating species may be either the $HO_2^{\cdot}$ radical or a complex of oxygen with the Sn^{2+} or Sn^{3+} ion. The kinetics of the oxidation of Sn^{2+} by oxygen has been investigated in an aprotic solvent (acetone), as well as the hydroxylation of cyclohexane under these conditions, in order to choose between these possibilities[154]. The $HO_2^{\cdot}$ radical cannot be formed during the oxidation of Sn^{2+} in acetone: thus cyclohexane is hydroxylated by tin-oxygen complexes, since the radical-ion O_2^-, formed by the transfer of one electron from the tin ion to oxygen, is devoid of hydroxylating power. The stoichiometry of the reaction in acetone is that one Sn^{2+} ion oxidises two oxygen molecules, which means that simultaneous transfer of two electrons from the tin(II) ion to oxygen, as is assumed by Ullrich, is impossible. The Sn^{2+} ion is oxidised by oxygen in two steps:

$$Sn^{2+} + O_2 \rightleftarrows \underset{(I)}{[Sn^{2+} \cdots O_2]} \rightleftarrows \underset{(II)}{[Sn^{3+} \cdots O_2^-]} \rightarrow Sn^{3+} + O_2^-$$
$$Sn^{3+} + O_2 \rightarrow \underset{(III)}{[Sn^{3+} \cdots O_2]} \rightarrow Sn^{4+} + O_2^-$$
$$O_2^- + O_2^- \rightarrow \text{Recombination} .$$

Such a scheme for the oxidation of Sn^{2+} in acetone is supported by the observed stoichiometry and also by the high rate constant of 100 $M^{-1}\ s^{-1}$ at 25 °C for the recombination of O_2^- radical-ions[178]. The O_2^{2-} ion is not usually formed in aprotic media, since it is stable only in aqueous solutions and in crystals[179]. Tin-oxygen complexes—$[Sn^{2+} \ldots O_2]$, $[Sn^{3+} \ldots O_2^-]$, or $[Sn^{3+} \ldots O_2]$—may possess hydroxylating power in an aprotic medium. It is difficult to choose between these three forms of activated oxygen; it is clear only that the activated oxygen in the complex has a radical character, since the hydroxylation of cyclohexane in acetone is retarded by the addition of inhibitors of radical reactions.

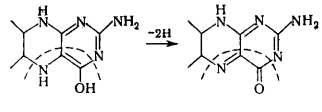
It is important to note that direct participation of the metal ion in hydroxylation and its effect on the distribution of isomers in the hydroxylation of aromatic compounds have been reliably established with other systems, e.g. Fe^{2+}–EDTA–O_2, so that the authors[145] speak of the hydroxylating power of the $[Fe^{2+} \ldots O_2]$ complex. Comparison of the distribution of isomers for a given substrate, e.g. toluene, obtained with oxygen and the Fe^{2+}, Sn^{2+}, Ti^{3+}, and Cu^+ ions shows that the isomeric composition of the cresols is strongly dependent on the metal ion[145]. If the radicals $HO_2^{\cdot}$, formed in the oxidation of all the above ions in aqueous solution, had been the hydroxylating species, the nature of the cation would not have influenced the distribution of isomers. Hence the hydroxylating species is a complex of the metal cation with oxygen, which shows variation in electrophilic strength on passing from one metal to another. The variation in the electrophilicity of species attacking the substrate is responsible for the difference in distribution of isomers. At high ionic concentrations the distribution becomes random—40 : 40 : 20—probably owing to a change in the mechanism of hydroxylation[145].

It is very important how an oxygen atom is transferred from the metal complex to the substrate. Hamilton noted that most reactions catalysed by mono-oxygenases and certain of their models are analogous to those of the very reactive carbenes CR_2 and nitrenes NR, which have six electrons around the carbon or nitrogen atom. Carbenes are incorporated at carbon-hydrogen bonds into aliphatic and aromatic compounds and add to alkenes to give cycloalkanes[138,143,180]. Reactions of the same type are accomplished by mono-oxygenases and their models. An oxygen atom, which has six electrons in the outer shell, may be the analogue of a carbene or a nitrene. However, oxygen cannot be generated in the enzymic processes. Hamilton therefore suggested that the oxygen atom is transferred to the substrate from an oxenoid complex, so called by analogy with carbenoids, which contain a combined carbene transferable to a substrate in the transition state. The oxygen molecule forms an oxenoid by interaction with a complex of the Fe^{2+} ion and a redox-active ligand such as ascorbic acid, tetrahydropteridine, etc. :



(IV)

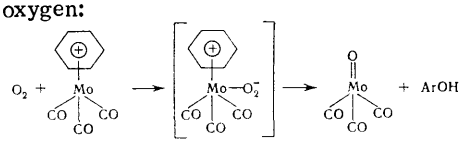
A complex similar to (IV) can be formed from tetrahydropteridine, involving the atoms segregated by the broken curve[138]:



The function of the Fe^{2+} ion in the complex (IV) consists in combining in the transition state with the reducing agent and oxygen to transfer electrons to the latter. In this complex (IV) transfer of a singlet oxygen atom from the bound oxygen molecule to the substrate probably becomes possible in such a way that radical intermediates are not formed. Transfer of a triplet oxygen atom to the substrate is energetically less advantageous, since a triplet product SO, less stable than the singlet product, would then be formed.

Hamilton's suggested oxenoid mechanism of oxygen transfer to a substrate explains satisfactorily the ability of mono-oxygenases to catalyse hydroxylation and epoxidation. The oxenoid complex may vary in electrophilicity depending on the nature of the metal and the ligand. Moreover, this complex, which attacks the substrate, may be radical or even nucleophilic in character. This property of the oxenoid complex helps us to understand the different distribution of isomers and the different orienting influence of substituents in the benzene ring on the hydroxylation of aromatic substrates. In individual cases the electrophilic character of the active centre in an enzyme system transmitting oxygen to an aromatic substrate can be assessed on the basis of model experiments. Thus the microsomal hydroxylation of toluene yields the isomeric cresols in the proportions 59 : 13 : 28, almost identical with the distribution obtained on hydroxylation with molecular oxygen in the presence of thiosalicylic acid and Fe^{2+} ions [144]. This suggests that the active centre of the microsomal hydroxylating system (cytochrome P-450) forms with molecular oxygen a complex which acts on the substrate as a moderately electrophilic reagent. The hydroxylation of toluene by such a strong electrophilic reagent as trifluoroperacetic acid gives the proportions 78 : 2 : 20 of isomeric cresols[161]. Hence the complex which attacks the substrate in the microsomal hydroxylating system is less electrophilic than trifluoroperacetic acid, which effects the same reaction.

A reaction has recently been investigated in which molecular oxygen and the substrate to be oxidised (benzene, naphthalene, or 2-methylnaphthalene) are activated simultaneously on the same active centre, a molybdenum atom[155, 156]. These aromatic compounds are oxidised by molecular oxygen neither under physiological conditions nor even at quite high temperatures. In the presence of a complex of molybdenum with carbon monoxide (hexacarbonylmolybdenum) in acetonitrile at 70–80°C, however, they undergo oxidation to phenols and naphthols. Arenes form with this carbonyl arenetricarbonyl complexes $ArHMo(CO)_3$ in which, as in hexacarbonylmolybdenum itself, the metal is present in the zerovalent state. The molybdenum atom is able to add an oxygen molecule and transmit to it one or more electrons, i.e. to activate molecular oxygen. At the same time the aromatic ligand in the arenetricarbonyl complex carries an effective positive charge, in contrast to the uncomplexed arene: i.e. it becomes capable of nucleophilic substitution. Thus the arene, having become more electrophilic, is attacked by oxygen, and the oxygen in the complex is more strongly nucleophilic than is free molecular oxygen:



The actual transfer of an oxygen atom to the aromatic molecule may be supposed to occur by Hamilton's "oxenoid" mechanism, with intermediate formation of a thermodynamically unstable arene epoxide, which isomerises into a phenol. Study of the kinetics of the hydroxylation of aromatic compounds in the $Mo(CO)_6$–O_2 system shows that oxygen is directly involved in the reaction: the rate of accumulation of phenols is directly proportional to the partial pressure of oxygen. With all the substrates the formation of phenols is preceded by that of the arenetricarbonyl complex $ArHMo(CO)_3$, which in the case of naphthalene limits the overall rate of the process. The ArH–$Mo(CO)_6$–O_2 system resembles "internal" mono-oxygenases in its type of action, since the oxygen atom not inserted into the substrate is stabilised by the metal, which is oxidised by the reaction. Unfortunately, the variation in reactivity of the aromatic molecules investigated in this system cannot be used to make deductions on the nature of the attacking species, since the complicated sequence of reactions is limited at different stages with different substrates.

It has recently been shown that peroxy-acids are capable of the oxygen-transfer reactions typical of mono-oxygenases [15, 108]. In several cases the products formed from the same substrate by the action of peroxy-acids are identical in character with those obtained by microsomal or microbiological oxidation [108, 167]. Thus identical products are obtained by the microsomal oxidation of 4-methyl-2,6-di-t-butylphenol and by its reaction with *m*-chloroperbenzoic acid. The sequence of changes undergone by naphthalene on oxidation with peracetic acid [167] is completely analogous to the microbiological transformation of this hydrocarbon by five different species of microorganisms [181]. As already noted, some mono-oxygenases do not contain metal ions, and activate oxygen by forming intermediates with the flavin components of the hydroxylating system. These intermediate compounds are essentially hydroperoxides [89–91, 129]. Peroxy-acids and certain other peroxy-compounds are therefore able to imitate the transfer of oxygen to a substrate characteristic of mono-oxygenases [108, 158–171, 173] (Table 4). It is very important to compare the rates of transfer of oxygen by peroxy-acids and by peroxy-derivatives of flavoproteins, which requires knowledge of the rate constants for reaction of such acids with various substrates. The reactions of peroxy-acids with alkenes have been characterised quantitatively [174], but no single rate constant had been measured until recently for their reactions with aromatic and aliphatic compounds. Only recently have determinations been made of the rate constants for the reactions of peracetic acid with naphthalene and with anisole [163, 167], which were measured in the presence of a mixture of acetic acid with dichloroethane or dichloromethane. The activation energies for peracetic acid with aromatic compounds are higher than in Prilezhaev's reaction, in good agreement with the increase in nucleophilic strength on passing from arenes to alkenes. An electrophilic peroxy-acid molecule undergoes a bimolecular reaction with a nucleophilic aromatic molecule, as with an alkene. No intermediate complex of a peroxy-acid with an aromatic molecule can be detected [163, 167]. The existence of such a complex has been proved kinetically for the reaction of peracetic acid with propene [182].

The bimolecular rate constants for the reactions of peroxy-acids with aromatic compounds show that the transfer of the oxygen atom from the acid to the substrate is quite rapid: thus at room temperature (20°C) the constant for trifluoroperacetic acid with naphthalene is 10^{-3} M^{-1} s^{-1} [163], while a molecule of 1-naphthol at the same temperature reacts with peracetic acid with a rate constant of ~0.33 M^{-1} s^{-1}. [163] Roughly similar rates are

observed for the reaction of hydroperoxy-derivatives of the flavin part of *p*-hydroxybenzoic hydroxylase with a 2,4-dihydroxybenzoate [90,91].

The autoxidising dihydroalloxazines [171], which react with oxygen to form hydroperoxy-derivatives, are similar to metal-free mono-oxygenases in their action on substrates which can be hydroxylated.

Peroxo-complexes of sexivalent molybdenum

(where L_1 and L_2 are ligands), discovered in the laboratory by Sajus [183], have recently been used [172,173] to simulate the transfer of oxygen by mono-oxygenases. Kinetic study of the interaction of such complexes having two ligands (L_1 = Hexametapol and $L_2 = H_2O$) and only one ligand L_1 has shown that both complexes form an intermediate compound with the substrate, which breaks down with the formation of glycidol. One molecule of the peroxo-complex epoxidises two molecules of allyl alcohol. The rate constants k_2* of decomposition of the intermediate complex have been determined at 50°C, together with the Michaelis–Menten constants

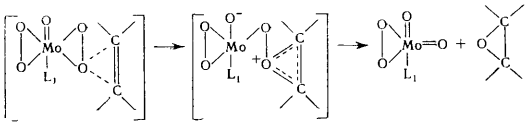
$$K_m = \frac{k_{-1} + k_2^*}{k_1}$$

where k_1 and k_{-1} are the rate constants of formation and dissociation of the intermediate complex. Table 5 gives the constants which we have obtained for both complexes at 50°C. The value $k_2 = 2.4 \times 10^9 \exp(-18300/RT)$ gave the enthalpy of activation as $\Delta H^{\neq} = 17.7$ kcal mole^{-1} and the entropy of activation as $\Delta S^{\neq} = -18.0$ cal mole^{-1} deg^{-1}. [172]

Table 5.

	K_m, M	k_2^*, s^{-1}
$MoO(O_2)_2L_1$	0.81	$9.71 \cdot 10^{-4}$
$Mo(O_2)_2L_1L_2$	0.78	$4.17 \cdot 10^{-4}$

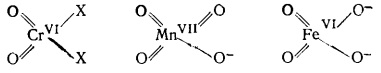
The closely similar quantitative data obtained for the two complexes and the steric hindrance to direct involvement of the molybdenum atom in interaction with the substrate suggest that the mechanism of the epoxidation of allyl alcohol by the molybdenum peroxo-complexes may be



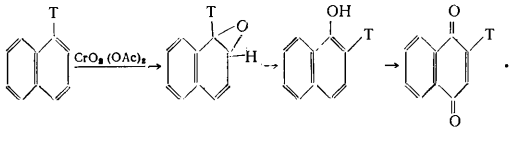
A significant feature of this mechanism is the involvement of the peroxo-oxygen atom in complex formation with allyl alcohol and the absence of direct involvement of the molybdenum atom in complex formation, which had been suggested by French workers [184]. The former mechanism is supported by the closely similar rate constants and values of K_m for the complexes with one and with two ligands, as well as by the good agreement between the activation functions of the limiting stage of the reaction and the thermodynamic functions of the epoxidation of allyl alcohol by other peroxide reagents that form a complex by means of the peroxide oxygen (Ref. 174, p. 1761).

It may be supposed, as in the above reaction scheme, that transfer of the oxygen atom to the allyl alcohol molecule takes place by an "oxenoid" mechanism. The electrophilic character of the epoxidising species is indicated by the ability of the peroxo-complex $MoO(O_2)_2L_1$ to hydroxylate naphthalene to 1-naphthol [173], the reaction being conducted in dichloroethane at 70°C. 1-Naphthol is an intermediate, undergoing further reactions with the peroxo-complex.

A team of American workers have emphasised the similarity between oxygen transfer by mono-oxygenases and by several oxo-compounds of metals of variable valency [185]

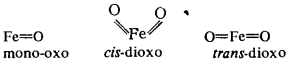


where X = OH, Cl, $OCOCH_3$. Indeed, chromyl acetate (X = $OCOCH_3$) epoxidises alkenes, potassium permanganate hydroxylates hydrocarbons [186], and chromyl chloride acetate accomplishes both reactions; oxo-compounds of lead $Pb(OCOCH_3)_{4-n}(N_3)_n$ are used for oxygenating the steroid androsta-4,9(11)-diene-3,17-dione, which is epoxidised and hydroxylated simultaneously [187]. It is well known also that the activity of a heterogeneous catalyst in oxidation is due to the presence of an M=O bond [188]. Oxygen transfer by such an oxo-compound as chromyl diacetate shows the surprising peculiarity that, in the hydroxylation of substituted aromatic substrates, this reagent can cause migration of a group from the position hydroxylated to a neighbouring position [185]:



Such migration of a substituent in an aromatic ring is very characteristic of the action of mono-oxygenases [189], and occurs in the hydroxylation of aromatic compounds by trifluoroperacetic acid [162]. Intermediate formation of arene oxides has been shown in the microsomal oxidation of aromatic compounds, without which the migration of substituents in aromatic compounds cannot be explained [162, 189–191].

Thus oxo-compounds of transition metals imitate an important feature of the action of mono-oxygenases. This suggested that in many other cases the species transferring oxygen to the substrate contains an oxo-group [185]; for example, the oxygen-transferring structures



are assumed for the iron ion. However, this hypothesis is not always confirmed in practice. The oxygen-carrying peroxo-complex of molybdenum $MoO(O_2)_2L_1$, where L_1 is hexametapol, contains two peroxo-groups and one oxo-group. Use for epoxidation of a complex labelled with the oxygen-18 isotope in the oxo-group gave an epoxide from which this isotope was absent: i.e. the oxo-group of the molybdenum(VI) complex plays no part in oxygen transfer [192]. Thus the oxo-form of the bond between metal and

oxygen is not universally present in all oxygen-transferring species.

All the reactions discussed in this Section simulate in some measure the transport of an oxygen atom to the substrate by mono-oxygenases. However, systems that generate free radicals can in no way be regarded as models, since active free radicals are incompatible with the living cell. Biochemical oxidations may involve not free radicals but their complexes with ions of metals of variable valency, e.g. complexes of HO· and HO_2· radicals with trebly charged iron ions. The study of models containing a metal ion or complex and oxygen shows that the most probable attacking species is a metal–oxygen complex. This is quite remarkable, since complex formation between oxygen and the active centre of mono-oxygenases (cytochrome P-450) has now been convincingly demonstrated. It has been shown by physical methods that the cytochrome binds the oxygen molecule by complex formation of the latter with an iron ion in the reduced state.

The study of model systems ($Fe^{2+} + O_2$, $Sn^{2+} + O_2$) has yielded numerous data confirming the hydroxylation of substrates by complexes of these ions with oxygen—involvement of the metal ion in hydroxylation, its effect on the distribution of isomers in the hydroxylation of aromatic substrates, absence of effect of added hydrogen peroxide on the reaction, the hydroxylation of arenes and the epoxidation of alkenes effected by the same system, which eliminates the HO· radical as attacking agent, the hydroxylation of substrates in aprotic media, where the formation of HO_2· is excluded, and other facts.

Hamilton's "oxenoid" mechanism appears the most probable and universal for transfer of an oxygen atom to the substrate, providing a satisfactory explanation of all experimental results obtained for model reactions and systems. The oxenoid mode of oxygen transfer most probably operates also with peroxide compounds such as peroxy-acids and peroxo-complexes of metals. These compounds well simulate oxygen transfer by mono-oxygenases having a flavin group in the active centre. Peroxy-acids, like mono-oxygenases, cause migration of a substituent from the position at which oxygen is inserted into the ring of an aromatic substrate to a neighbouring position.

The intense study of the reactions of mono-oxygenases, the isolation and purification of this group of enzymes, the investigation of the structure and the functions of component parts of the composite enzyme system, the wide use of physical methods in studying the state of the metal ion in the active centre: all this has in many cases established great certainty as to the mechanism of the action of these enzyme systems. Investigations of the prestationary and steady-state kinetics of the reactions of various mono-oxygenases have played a very important part in establishing the mechanisms discussed in this Review. However, even such a frontal attack by research workers in this field has not revealed the ultimate mechanism of the activation of molecular oxygen. Not only study of the action of the mono-oxygenases themselves but also detailed study of model systems have played a great part in elucidating individual features of this mechanism. Examination of models will enable us to ascertain the structure of the species transferring oxygen to the substrate, and perhaps indicate ways in which oxygen may be chemically activated under physiological conditions. The yields of reaction products obtained by means of model systems are still quite low, but systems have been found enabling us to follow the kinetics of the accumulation of reaction products and the valency changes undergone by metal ions occupying a leading role in these systems.

The practical value of mono-oxygenase enzymes is very great for the most diverse fields of toxicology, pharmacology, and oncology. Recent results threaten a revolution in the synthesis of several physiologically active substances. Thus 11 β-hydroxylase and Δ^{1-2}-dehydrogenase have recently been used to effect the two-step transformation of the readily available Reichtein's substance S into prednisolone [193]. This conversion is achieved by means of enzymes fixed on gel matrices and placed in two columns connected in series. Hydroxylation of substance S to cortisol takes place in the first column, and dehydrogenation to prednisolone in the second column. It may be hoped that the number of examples of such transformations by means of mono-oxygenase enzymes will increase.

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Silicon-containing Ureas

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In the review an attempt is made for the first time to survey studies on the synthesis, properties, and likely practical applications of silylureas. In view of the significant differences in the methods of their synthesis and properties, *N*-silylureas are examined separately from the carbofunctional compounds in which the urea moiety and the silicon atom are separated by a group of atoms.
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I. INTRODUCTION

Urea (carbamide) and its derivatives are some of the most widely used organic compounds. In recent years there has been a vigorous development of the chemistry of organic derivatives of the elements based on urea and in particular of its organosilicon derivatives. The introduction of an organosilyl substituent into the urea molecule alters sharply its physical and chemical properties. This applies especially to N-silyl derivatives. In particular, the hydrogen bonds are greatly weakened, which has found practical applications in the chromatography and separation of many urea derivatives. The high silylating capacity of *N*-silylureas has made them some of the most important auxiliary reagents in organic syntheses. There are good prospects also for practical applications of polymeric materials based on silicon-containing ureas.

N-Silylureas are of independent interest for the development of theoretical ideas on the tautomerism of amides, since, in contrast to organic derivatives of urea and amides, many physical properties of these compounds suggest that they exist in both the amide and isoamide forms.

II. *N*-SILYLUREAS

1. METHODS OF SYNTHESIS

a. Interaction of Silanes and Halogenosilanes with Ureas

The NH group in amines is known to react with halogenosilanes to form the corresponding *N*-silyl derivatives. However, this reaction is greatly hindered in the presence of the C=O group next to the amino-group[1-3], as happens in ureas, amides, urethanes, semicarbazides, and other similar compounds. When urea is acted upon by triorganohalogenosilanes under moderately mild conditions, silicon-substituted ureas are not formed[2,3] and the latter can be obtained only when metallated urea derivatives are used[4]:

$$Me_3SiCl + K[NHCONH_2] \rightarrow Me_3SiNHCONH_2 + KCl ,$$

or when the reaction is carried out in the presence of hydrogen halide acceptors[5-7].

Under severe conditions, the interaction of triorganohalogenosilanes with urea apparently leads to the formation of isocyanatosilanes in consequence of the decomposition of the intermediate quaternary salts[8]:

$$R_3SiCl + H_2N\overset{\overset{O}{\|}}{C}NH_2 \rightarrow [R_3SiNH_2\overset{\overset{O}{\|}}{C}NH_2]^+Cl^- \rightarrow R_3SiN{=}C{=}O + NH_4Cl$$

(when R = Ph, the reaction was carried out in the melt and for R = Me in an autoclave at 280–300°C).

When organotrihalogenosilanes, $SiCl_4$, and $SiBr_4$, react with urea or its alkyl and aryl derivatives, only hydrolytically unstable complexes are formed, for example[9,10]:

$$SiCl_4 \cdot 6H_2NCONH_2;\ SiBr_4 \cdot 6H_2NCONH_2;\ Si_2Cl_6 \cdot 10H_2NCONH_2$$
$$SiCl_4 \cdot 6H_2NCONHMe;\ SiCl_4 \cdot 6H_2NCONHPh;\ SiCl_4 \cdot 6H_2NCONMe_2.$$

The complexes do not have a distinct melting point and decompose into the initial components on dissolution in organic solvents, subliming with decomposition on heating to 150–200°C. The replacement of a halogen atom in silicon tetrahalide by an alkyl or alkoxy-group (but not by a hydrogen atom) reduces the coordination number with respect to urea by unity[10]:

$$MeSiCl_3 \cdot 5H_2NCONH_2;\ PhSiCl_3 \cdot 5H_2NCONH_2;\ SiHCl_3 \cdot 6H_2NCONH_2 .$$

The type of bond in the complexes formed has been studied inadequately because of the difficulties in the determination of their molecular weight and conductivity and in carrying out an exact X-ray diffraction analysis due to the decomposition of the complexes in solution and on fusion and also because of the difficulty of growing their crystals. X-Ray diffraction analysis of $SiCl_4.6H_2NCONH_2$ powder indicates a cubic crystal lattice with 7.79 Å faces[10]. The adducts of other halogenosilanes with urea have a similar lattice, which in the case of $SiBr_4$ has somewhat greater dimensions (8.11 Å). Bearing in mind the branching and considerable bulk of halogenosilane molecules and also the polarity of the silicon–halogen bond, the formation of clathrate compounds of the lattice type channel variety (the channel diameter is usually 5.1 Å), in which the halogenosilane molecule would be located within the crystal lattice of urea, is unlikely. The large number of urea molecules per halogenosilane molecule also rules out the possibility that they are incorporated as additional electron-donating ligands in the inner

sphere of the complex, partly with retention of Si–Cl bonds, as happens, for example, in the complex $SiCl_4 \cdot C_5H_5N$.[9]

On the basis of infrared spectra, which indicate a weakening of the N–H bond in the adducts, and also the identical compositions of the complexes of halogenosilanes with urea and *NN*-dimethylurea (1 : 6 in both cases for $SiCl_4$), it has been suggested[10] that ureas are linked to halogenosilanes only by one of the two amino-groups, while the other is probably involved in the formation of a hydrogen bond with another urea molecule.

In contrast to halogenosilanes, monoalkylsilanes $RSiH_3$, starting from n-hexylsilane, and di-n-alkylsilanes R_2SiH_2, starting from diethylsilane, form with urea true crystalline clathrate compounds[11–13]. In the first case the $RSiH_3$ molecules are located in the channels of the hexagonal crystal lattice of urea, like carboxylic acids, in the form of oriented double molecules[13]. The occluded di-n-alkylsilane molecules are distributed in a sequence, like their hydrocarbon analogues (paraffins)[11]. The lowest members of the above series do not form adducts with urea even at low temperatures (–15°C). Both types of clathrate compounds (with $RSiH_3$ and R_2SiH_2) are less stable than the analogous paraffin compounds, which is manifested by their dissociation into the initial components at a lower temperature. Unbranched di-n-alkoxysilanes form with urea analogous but more stable clathrate compounds[14]. Thioureas do not form adducts with the above organosilicon compounds[13,14].

Unbranched silanes such as trisilane, tetrasilane, and others (in contrast to the branched isomers) form clathrate compounds with both urea and thiourea[15], which are stable in air below their dissociation temperatures (–15°C for Si_3H_8 and 5°C for Si_4H_{10} in the adducts with urea). The stability of the adducts increases with increases in the silane chain length and falls on passing to urea and thiourea.

The clathrate compounds of higher silanes (starting from Si_5H_{12}) are stable even at room temperatures and the silanes in such compounds lose their capacity for self-ignition in air. In terms of their relative stabilities, compared with other organic and organosilicon clathrate compounds, they occupy the last place[15]: aliphatic acids > paraffins > di-n-alkoxysilanes > di-n-alkylsilanes > mono-n-alkylsilanes > silanes. The molecular diameters of certain types of silanes and their ability to form clathrate compounds with urea are indicated in the Table[11].

The formation of clathrate compounds by halogenosilanes with urea.

Silane	Molecular diameter		Formation of clathrate compounds	Silane	Molecular diameter		Formation of clathrate compounds
	max.	min.			max.	min.	
$RSiH_3$	5.1	4.3	+	$RSiCl_2R$	6.7	5.4	—
$RSiH_2R$	5.1	4.3	+	$RSiH_2OMe$	5.1	4.3	+
$RSiHCl_2$	6.6	5.4	—	$RSiH(OMe)_2$	8.5	4.3	—
$RSiCl_2$	6.6	5.7	—	$RSiH(OMe)R$	8.5	4.3	—
$RSiHClR$	6.6	5.4	—	$RSiH_2Cl$	5.3	4.3	*

Note: the + and – signs denote that the clathrate compounds are or are not formed; the asterisk (*) shows that the clathrate compounds can be formed in a non-solvating medium.

The selectivity of the action of urea with respect to normal (unbranched) silanes can be used for the preparative separation or purification of a mixture of normal silanes and isosilanes[15] as well as their alkyl and alkoxy-derivatives[11].

b. Transamination Reactions

The transamination reaction by Larsson's method[16], applied for the first time to the silylurea series in 1959 by Benneville and coworkers[5,17], proved to be a convenient procedure for the introduction of an organosilyl residue into urea with formation of the Si–N bond:

$$H_2NCONH_2 + Me_3SiNHCMe_3 \xrightarrow[12\,h]{110^\circ} Me_3SiNHCONH_2\,(89\%) + Me_3CNH_2 ,$$

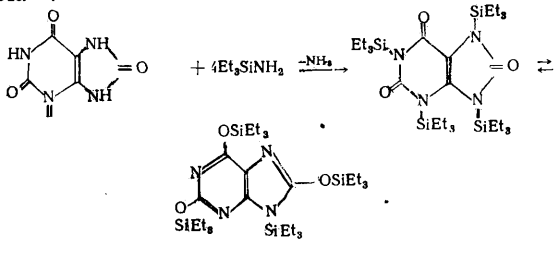
$$MeNHCONHMe + Me_3SiNHCMe_3 \rightarrow Me_3SiNCONHMe + Me_3CNH_2 .$$
$$\quad\quad\quad

resulting monotrimethylsilylacetamide can be readily removed at the end of the reaction by vacuum distillation[27].

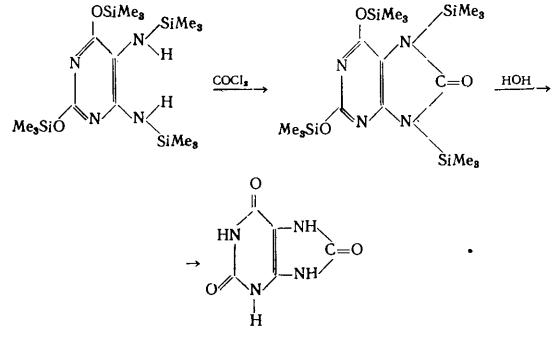
It is noteworthy that the possibility of the rapid and quantitative silylation of urea, amines, amides, and other compounds with extensive hydrogen bonding is important for organic and biological chemistry, since it makes it possible to convert high-melting non-distilling and sparingly soluble compounds into stable and volatile silyl derivatives, which are readily soluble in organic solvents and are susceptible to separation and chromatographic analysis[28,31]. The introduction of the trimethylsilyl residue as a temporary protecting group is extensively used in a wide variety of organic syntheses[32-35].

N-Silylureas, particularly those of the aromatic series, are themselves powerful silylating agents like carboxylic acid silylamides[22,25,26,36] (see also the chemical properties of *N*-silylureas). *NN'*-Diphenyl-*N*-trimethylsilylurea is particularly suitable as a donor of the trimethylsilyl group[22].

The resulting diphenylurea does not dissolve in the majority of organic solvents and therefore can be readily removed from the reaction mixture by filtration. The insolubility of diphenylurea is apparently also the reason why the equilibrium in silyl–proton exchange reactions is in this case almost wholly displaced to the right. Silylureas which could not be obtained with the aid of HMDS[18] are readily formed when a mixture of *NN'*-diphenyl-*N*-trimethylsilylurea is stirred with the corresponding urea derivative in acetonitrile at 30–35°C.[22] The reaction reaches completion in the course of several minutes or several hours for particularly sparingly soluble compounds. In particular, *NN'*-bis(trimethylsilyl)thiourea and *NN*-dimethyl-*N'*-trimethylsilylurea were obtained in this way in yields of 82 and 79% respectively. A series of cyclic analogues of urea were also synthesised by the silylation of the amide group. Thus, when uric acid is heated in triethylaminosilane, tetra(triethylsilyl)uric acid, which can exist in both lactam and lactim forms, is formed in 90% yield[37]:



When 5,6-diaminouracil reacts with HMDS, the product is 2,4-bis-(*O*-trimethylsilyl)-5,6-bis(trimethylsilylamino)-uracil, which cyclises on reaction with phosgene to form a uric acid derivative[38]; the latter cannot be obtained without using a silyl protecting group:



c. Reactions of Isocyanatosilanes with Amines

Organosilicon derivatives of urea of different structures, $R_3SiNHCON\langle$, $R_2Si(NHCON\langle)_2$, $RSi(NHCON\langle)_3$, and $Si(NHCON\langle)_4$ (where R = alkyl, aryl, or alkoxy-group), are as a rule formed in high yields by the reaction of the corresponding mono- or poly-isocyanatosilanes with aliphatic and aromatic primary and secondary amines†[18,39-50], for example:

$$Me_3SiN{=}C{=}O + Et_2NH \xrightarrow{55-60^\circ} Me_3SiNHC(=O)NEt_2 \quad (91\%)\ .$$

Exceptions are amines of low basicity (diphenylamine, HMDS) which do not react with Me_3SiNCO even under severe conditions[41], and the reaction of H_3SiNCO with NH_3 at −78°, which leads to the formation of monosilanes SiH_4 and an involatile solid residue[48].

Amines can be arranged in the following sequence in terms of their reactivities in the reaction with isocyanatosilanes[40]: $AlkNH_2 > Alk_2NH > ArNH_2 > ArNHR > Ar_2NH$. In the series of isocyanatosilanes $Si(NCO)_4$ is more reactive than in its alkyl and aryl derivatives[41,45,49].

Silylsemicarbazides were obtained by the reaction of isocyanatosilanes with hydrazines[21]:

$$Me_3SiN{=}C{=}O + H_2NNH_2 \rightarrow H_2NNHC(=O)NHSiMe_3 \quad (90\%)\ .$$

d. The Interaction of Aminosilanes and Silazanes with Organic Isocyanates

Reactions with monoisocyanates. The reactions of organoaminosilanes and silazanes with organic isocyanates, discovered in 1964 independently by several groups of workers (Zhinkin[52], Klebe[53], Oertel[54,55], and Fink and coworkers[56-58]), constitute a convenient method for the preparation of *N*-silylureas. According to the reports of Wannagat and coworkers[18,21,59,60] concerning the interaction of organic isocyanates with compounds containing simultaneously Si–N and N–H bonds (silylamines, silylhydrazines, and silylhydroxylamines) published before 1964, it was believed that the reaction involves only the N–H bond with migration of the hydrogen atom to the nitrogen atoms of the isocyanate group, for example:

$$(Me_3Si)_2NH + PhNCO \rightarrow (Me_3Si)_2NCONHPh\ .$$

However, the evidence quoted in this connection for the structure of the resulting compound, i.e. data obtained from their hydrolysis to the corresponding organic urea derivatives, cannot be regarded as convincing, since even when the reaction involves the Si–N bond, hydrolysis should yield the same results owing to the silyl–proton exchange in the *N*-silylureas[53].

A detailed study of this reaction by the above workers[26-36,52-58,61-65] and primarily by Zhinkin and coworkers[52,61-63,66,67] showed that organoaminosilanes and silazanes containing not only primary but also secondary and tertiary hydrogen atoms, i.e. compounds without N–H bonds, react with isocyanates. When Si–N and N–H bonds are present

† In early studies on reactions of isocyanatosilanes with amines it was concluded erroneously that the reaction proceeds via the elimination of the silyl group with formation of organic urea derivatives[49,51].

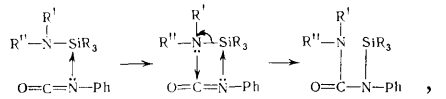
simultaneously, the latter does not take a direct part in the reaction with isocyanate, which involves preferentially the Si–N bond. The only exception‡ is the reaction of isocyanates with aminosilanes containing a primary nitrogen atom, which was shown by a study of the structure of the final product to proceed via the classical isocyanate condensation mechanism, i.e. with migration of the hydrogen atom from the nitrogen atom of the aminosilane to the nitrogen atom of the isocyanate group[62,66,70]:

$$R_3SiNH_2 + PhNCO \rightarrow R_3SiNHC(O)NHPh \quad (R=Et, Bu, Ph) .$$

When other organoaminosilanes and organosilazanes react with isocyanates in 1 : 1 proportion, the Si–N bond dissociates and the triorganosilyl group migrates to the nitrogen atom of the isocyanate with formation of organosilicon urea derivatives[26,36,52–56,58,61–63,66,71,72]:

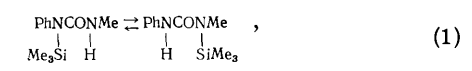
$$R_2NSiMe_3 + R'NCO \rightarrow R_2NC(O)N(R')SiMe_3 ,$$
$$(Me_3Si)_2NH + R'NCO \rightarrow Me_3SiNHC(O)N(R')SiMe_3 ,$$
$$RNHSiMe_3 + R'NCO \rightarrow RNHC(O)N(R')SiMe_3 ,$$
$$(Me_3Si)_2NR + R'NCO \rightarrow Me_3SiN(R)C(O)N(R')SiMe_3 .$$

The reaction mechanism apparently involves the formation of an unstable complex comprising four units, in which the shift of electron density to the nitrogen atom of the aminosilane or silazane weakens the Si–N bond and leads to its dissociation as well as the dissociation of the C=N π bond in the isocyanate group[63,66,73,74]:



where R′ = H or alkyl and R″ = H, alkyl, aryl, or SiR_3.

It follows from ^{1}H NMR data that silylureas with a proton and a triorganosilyl group at the N and N′ atoms respectively can be involved in the presence of a solvent in intramolecular (Scheme 1) or intermolecular (Scheme 2) proton–trimethylsilyl exchange[53]:



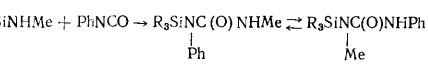
(1)

(2)

Depending on the solvent and the nature of the groups at the silicon and nitrogen atoms, the equilibrium can be displaced towards one of the isomers.

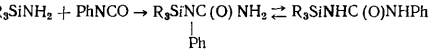
The occurrence of silyl–proton exchange was also confirmed by a study of the products of the addition of optically active *N*-(methylphenyl-α-naphthylsilyl)methylamine to phenyl isocyanate[73,74]. It was shown that the reaction proceeds with retention of the configuration at the silicon atom (its stereospecificity is greater than 90%) and the resulting optically active silylurea (IIIa) undergoes rapid racemisation in tetrahydrofuran (THF) solution and slow racemisation in benzene solution, the latter being greatly accelerated on heating§.

After compound (IIIa) has been allowed to stand for many hours, its ^{1}H NMR spectra show that it has been converted into (IIIb) as a result of the intermolecular exchange of the Me_3Si groups:

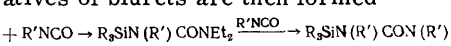


where R_3Si = (c-$C_{10}H_7$)(C_6H_5)(CH_3)Si.

In view of the possibility of the silyl–proton exchange in silylurea, one cannot rule out the possibility that the above anomalous reaction (in the series of reactions of isocyanates with aminosilanes) with primary aminosilanes[62,66,70] in reality involves the Si–N bond and not the N–H bond, the final reaction product being formed as the result of the fast intermolecular or intramolecular silylation of the *N*-phenyl-*N*-trimethylsilylurea produced initially, which is in the present case facilitated by the presence of the free NH_2 group:



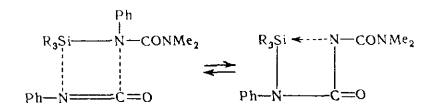
N-Silylureas formed on interaction of equimolar amounts of isocyanate and aminocyanate (or silazane) can readily enter into further reaction with the excess isocyanate and, depending on whether the urea contains only Si–N bonds or both Si–N and N–H bonds, the reaction proceeds in different ways. Silylureas without N–H bonds, obtained from tertiary silylamines R_2NSiMe_3, react with isocyanate in the same way as the initial silylamines, i.e. with migration of the triorganosilyl group to the nitrogen atom of the isocyanate. High yields of the corresponding silyl derivatives of biurets are then formed[36,57,63–65]:



The same compounds can be obtained also when an excess of isocyanate reacts directly with tertiary silylamines[63].

When silylbiurets are heated (for example in the course of their distillation), they decompose into the initial components[57], so that, depending on the temperature conditions, the compounds can be in equilibrium with the initial silylurea and isocyanate, the equilibrium can be established several times but does not result in racemisation[74].

A mechanism similar to that for the reaction of isocyanates with aminosilanes was proposed for the formation of silylbiurets and the reverse reaction involving the elimination of the isocyanate[74]:



The Si–N bond in silylbiurets is more resistant to hydrolysis than in silylureas and further reaction involving this bond with the excess isocyanate does not proceed or proceeds with difficulty[57]. Fink explains this finding by

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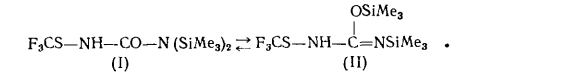
‡ According to Haas's data[68,69], the reaction of trifluoromethylsulphenyl isocyanate with HMDS also involves the cleavage of the N–H bond and not the Si–N bond:

$$(Me_3Si)_2NH + F_3C(S)NCO \rightarrow F_3C(S)NHC(O)N(SiMe_3)_2 .$$

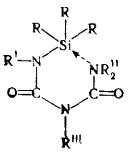
Although the ^{1}H NMR spectrum of the resulting urea has two kinds of resonances due to the Me_3Si groups, like *NN*-bis-silylamides, the authors attribute this to the hindered rotation about the C–N bond and believe that the product has structure (I) and not (II):



This conclusion was also confirmed by infrared spectroscopic data.

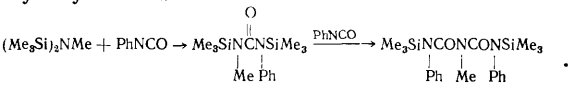
§ Kaufmann et al.[74] showed for the 1 : 1 adduct of PhNCO and the optically active silylamine (α-$C_{10}H_7$)(C_6H_5)(CH_3)SiN.$(CH_3)_2$ that silylureas without N–H bonds do not racemise.

the stabilisation of the molecule due to intramolecular coordination with formation of the following stable cyclic structure[57,64]:

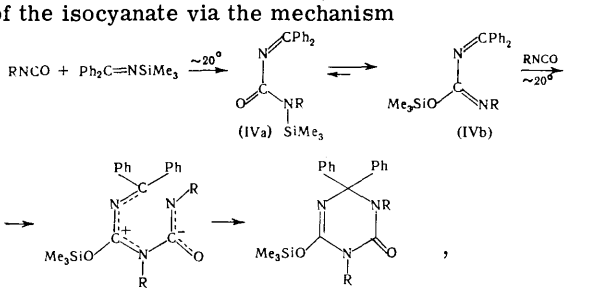


Since these compounds regenerate free isocyanate on heating and exhibit all the reactions characteristic of the isocyanate group, they have been patented as "latent" isocyanates, which are less susceptible to hydrolysis and are less volatile than free isocyanates[64].

Silylureas without N–H bonds, formed from *N*-alkylsilazanes, react with isocyanates via the same mechanism as tertiary silylamines[52,53,62,63,66]:

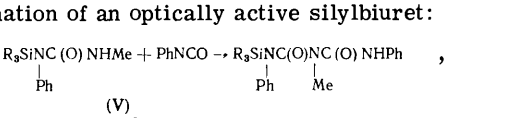


The interaction of isocyanates with diphenylmethylene-*N*-trimethylsilylamine proved to be specific[75]. For a 1 : 1 reactant ratio, the reaction proceeds selectively with cleavage of the Si–N bond to give silylureas, but, in the presence of an excess of the isocyanate, the products are not silylbiurets, as usually happens, but triazinone derivatives. The authors[75] explain this by 1,4-cycloaddition of the isomeric (imide) form of silylurea (IVb) to the C–N bond of the isocyanate via the mechanism

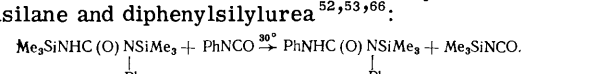


where R = Me, Ph, or PhC(O). This reaction confirms the possibility of the existence of silylureas in the isoamide form. The occurrence of the tautomeric equilibrium (IVa) ⇌ (IVb) has also been confirmed by a study of the temperature-induced changes in the ^{1}H NMR spectrum of compound (IV).[75]

The mode of reaction involving ureas containing both Si–N and N–H bonds has been studied inadequately, in many cases not at all owing to the instability of the addition products. Thus, according to the data of Kaufmann et al.,[73] when an excess of isocyanate is allowed to react with the optically active silylurea (V), the reaction involves the N–H bond with retention of the configuration and the formation of an optically active silylbiuret:



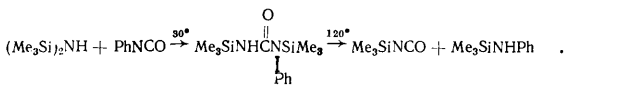
However, in the case of the silylurea containing the N–H bond and obtained from HMDS and PhNCO (1 : 1), further reaction with a second isocyanate molecule under the same mild condition leads to the formation of isocyanatotrimethylsilane and diphenylsilylurea[52,53,66]:



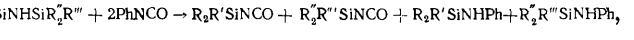
The same products were isolated also after the direct interaction of HMDS with PhNCO in proportions of 1 : 2.[52,63,66]

At an elevated temperature the composition of the products of the reaction of aminosilanes with isocyanates is as a rule anomalous, which is evidently due to the thermal instability of the intermediate silylureas, their tendency towards tautomeric transformations, and a number of other factors.

Thus at about 120°C HMDS reacts with PhNCO to form Me_3SiNCO and $PhNHSiMe_3$.[61,66] Since the same products are formed on heating *N*-phenyl-*NN'*-bis(trimethylsilyl)urea to 120°C,[61] the reaction evidently proceeds via the intermediate formation of this compound:

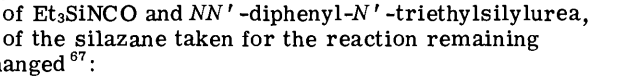


Other hexaorganodisilazanes, with the exception of hexaethyldisilazane, react similarly with PhNCO at elevated temperatures, silazanes containing different groups at the silicon atoms forming two isocyanates and two triorganosilylamines in approximately equal amounts[67]:

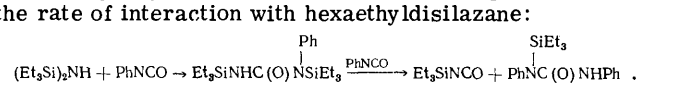


where R and R'' = Me or MeO and R' and R''' = Me, MeO, or Ph. The nature of the organic group linked to the silicon atom does not have a significant influence on the course of this reaction.

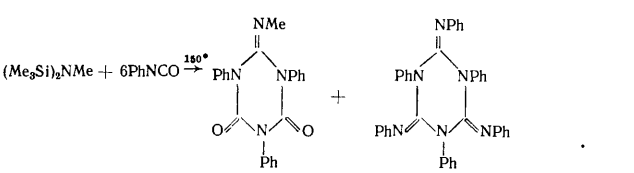
Hexaethyldisilazane reacts differently with PhNCO. Regardless of the temperature conditions, the interaction of equimolar amounts of the reactants leads to the formation of Et_3SiNCO and *NN'*-diphenyl-*N'*-triethylsilylurea, half of the silazane taken for the reaction remaining unchanged[67]:



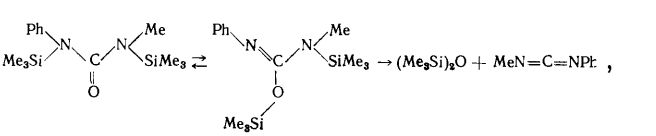
The authors[67] explained this course of reaction by the fact that the rate of interaction PhNCO with *N*-phenyl-*NN'*-bis(triethylsilyl)urea formed in the first stage is faster than the rate of interaction with hexaethyldisilazane:



The reaction of isocyanates with *N*-alkylated disilazanes at elevated temperatures is unusual. For example, Itoh et al.[76] showed that heptamethyldisilazane reacts with an excess of PhNCO to form the triazine derivatives (VI) and (VII):

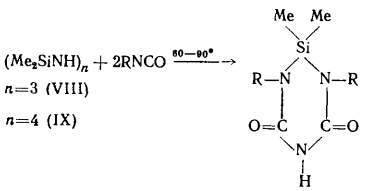


They suggest that the formation of (VI) is due to the β-elimination of the iso-form of the initial silylurea (1 : 1 adduct) to give methylphenylcarbodiimide:



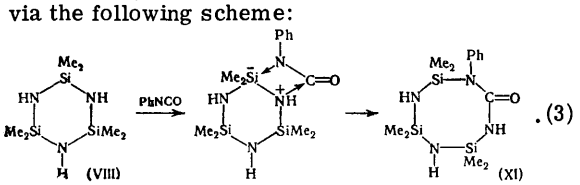
which then undergoes a cyclisation reaction with two molecules of PhNCO to give compound (VI). The formation of compound (VII) can be accounted for in two ways: (1) the 1 : 2 adduct of heptamethyldisilazane with PhNCO undergoes a similar decomposition (with decarboxylation) to diphenylcarbodiimide, which then trimerises and (2) PhNCO is decarboxylated with subsequent trimerisation of the resulting diphenylcarbodiimide.

Fink showed [56,77,78] that the interaction of organic isocyanates with cyclic silazanes proceeds in the same way as the interaction with silylamines via the Si–N bond, while in the presence of the N–H bond the latter is not involved in the reaction. Thus the cyclosilazanes (VIII) and (IX) react vigorously with organic isocyanates, forming derivatives of 1,3,5-triaza-2-silacyclohexanediones [56,77,78], which are cyclic analogues of silylbiurets:

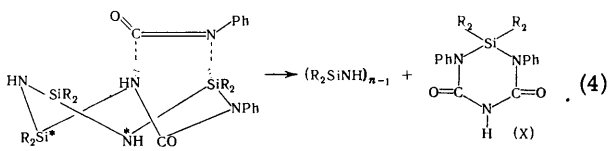


The structures of the compounds obtained were demonstrated by hydrolysis (when R = Ph, 1,5-diphenylbiuret is formed), ^{1}H NMR spectra, and X-ray diffraction [79].

According to the proposed reaction mechanism [56,77], there is initially a cycloaddition to the Si–N bond of the silazane via the following scheme:

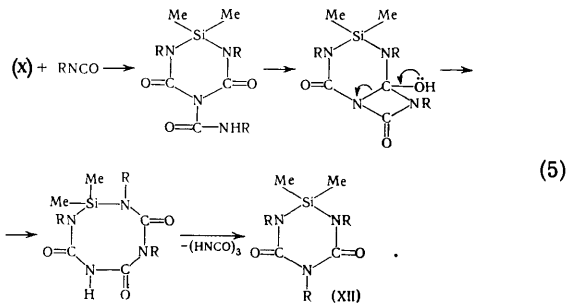


The heterocycle (XI) formed can react further in two ways: by combining with another molecule of PhNCO via the Si–N bond adjoining the PhN–Si group or it can react via Scheme 4, where the transannular interaction between the Si* and N* atoms lead to ring contraction and the elimination of cyclosilazane:



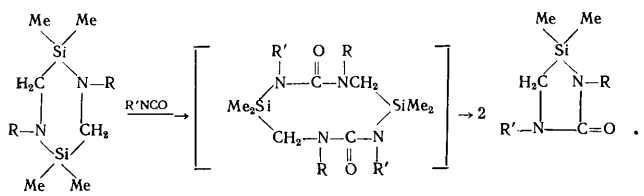
When an excess of the isocyanate (in relation to two moles of PhNCO per Me_2SiNH structural unit) is used, the number of moles of compound (X) formed is inconsistent with the theoretical value. Depending on the ratio of the initial reactants and the type of silazane, a greater or smaller amount of unidentified product is formed, which has been interpreted as supporting a stepwise reaction involving the Si–N bonds of the silazane, since the formation of such products on simultaneous reaction via all the Si–N bonds could not be explained.

At an elevated temperature (120–160°C) further reaction of the isocyanate with 1,3,5-triaza-2-silacyclohexanediones (X) or the direct reaction of cyclosilazanes with a large excess of the isocyanate leads to the formation, via a stage in which unstable macrocyclic compounds are produced, of 1,3,5-trisubstituted derivatives of 2,2-dimethyl-1,3,5-triaza-2-silacyclohexanediones (XII) [56,77]. The reaction can be regarded as cycloaddition to the RNSi–N bond in accordance with Eqn. (3) or as transacylation by the isocyanate [reaction (5)] via the formation of an eight-membered ring with subsequent elimination of cyanuric acid:



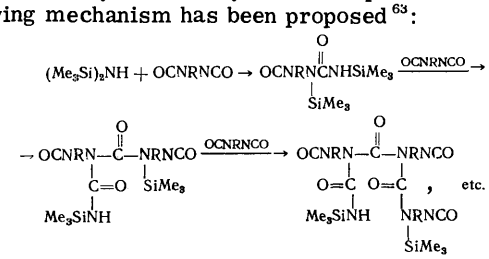
The use of an excess of diisocyanate in this reaction leads to compounds (XII) with free NCO groups [56,80,81] [for example, R-3-NCO-4-MeC_6H_3, $-(CH_2)_6NCO$, or $-C_6H_4CH_2C_6H_4NCO$ respectively for *p*-tolylene, hexamethylene, and diphenylmethylene diisocyanates].

Cyclic aminosilanes, derived from the recently discovered heterocyclic 2,5-disilapiperazine system [82], react vigorously with isocyanates to form five-membered silacycloureas. Ten-membered products resulting from the insertion of two molecules of isocyanate, which rearrange to five-membered rings by virtue of the ease of the transannular interactions between the Si and N atoms, are evidently formed in the first stage [82]:

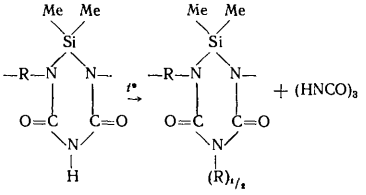


Reactions with di-isocyanates. The reactions of organoaminosilanes and silazanes with diisocyanates proceed similarly to the reactions with these compounds with monoisocyanates and lead to the formation of monomeric or polymeric silylureas and silylbiurets depending on the conditions, the reactant ratio, and the functional groups in the aminosilane [63,66,78,83–87], aromatic diisocyanates being more reactive than aliphatic diisocyanates [66].

It has not been possible to achieve the reaction between hexamethylene diisocyanate and HMDS [63]. At 30–35°C there is no interaction and at 80°C the diisocyanate polymerises. Under these conditions, HMDS is completely recovered from the reaction. When an excess of the diisocyanate (up to tenfold) is used, a polyisocyanate is also formed. Evidently at elevated temperatures HMDS behaves merely as a catalyst for this process. The following mechanism has been proposed [63]:

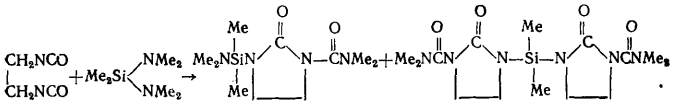


The reaction of hexamethylcyclotrisilazane with diisocyanates at 110°C leads to the formation of transparent, elastic, linear polymers with structural units (XIII), which decompose on heating above 110°C with elimination of cyanuric acids, giving cross-linked polymers with the structural units (XIV), exhibiting a high resistance to the action of acids[77]:



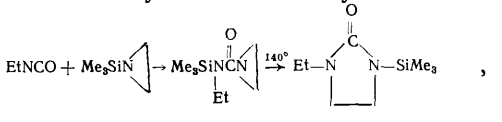
(XIII) (XIV)

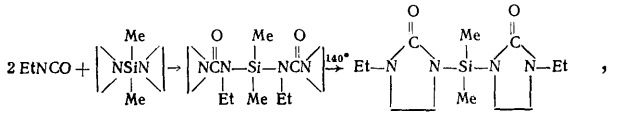
An interesting reaction with formation of cyclic silylurea derivatives (*N*-silylimidazolidinones) was discovered by Scherer and Schmidt[88]:



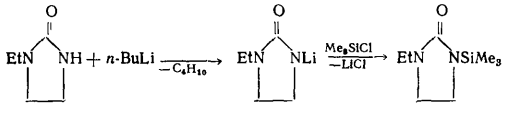
(70%) (20%)

According to the data of the same workers[89], derivatives of *N*-silylimidazolidinone can be obtained also in a different way: by a thermal rearrangement with the expansion of the rings of the silylureas formed in the reaction between monoisocyanates and *N*-silylaziridines:

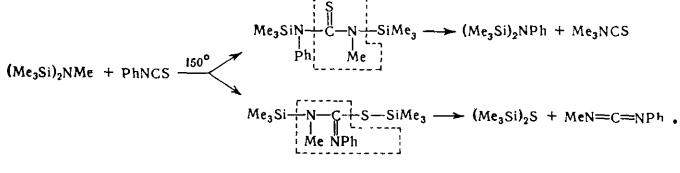




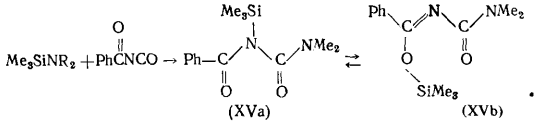
or via the lithio-derivative of imidazolidinone:



Reactions with isothiocyanates. The addition of silylamines and silazanes to isothiocyanates[53-55,57,61,62,66,74,90] proceeds via the same mechanism as the addition to isocyanates but much less vigorously[66,90] and leads to the corresponding organosilicon thiourea derivatives. It has been shown for the reaction of hexamethyldisilazane with PhNCS[90] that, in contrast to isocyanates, under severe conditions there is a possibility of addition not only to the C=N but also the C=S bond, which has been confirmed by the composition of the decomposition products of the intermediates:

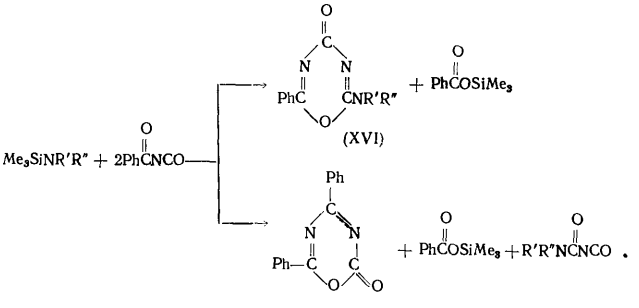


Reactions with acyl isocyanates. A characteristic feature of the reaction of aminosilanes with acyl isocyanates consists in the ability of the latter to be involved not only in 1,2- but also in 1,4-addition. Thus the reaction of dialkyl-*N*-trimethylsilylamines and benzoyl isocyanate in proportions of 1 : 1 gives a high yield of *NN*-dialkyl-*N'*-benzoyl-*N'*-trimethylsilylurea (1,2-addition), which is believed to be involved in the tautomerism (XVa) ⇌ (XVb) on the basis of ^{1}H NMR data[91-93]:



(XVa) (XVb)

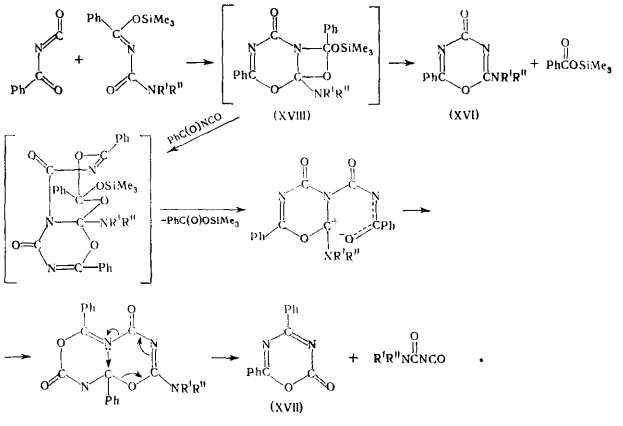
When a second acyl isocyanate molecule acts on the resulting urea or the silylamine reacts with two moles of the acyl isocyanate, the products are (in contrast to the reaction with isocyanates) derivatives of oxadiazinone [(XVI) and (XVII)], benzoyloxytrimethylsilane, and *NN*-dialkylcarbamoyl isocyanate and not silylbiurets:



(XVI)

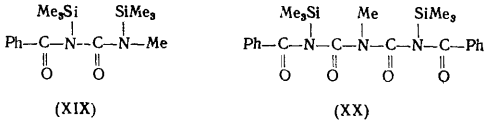
(XVII)

This reaction is regarded as proof of the existence of the iso-form of silylurea. The formation of the oxadiazinones (XVI) and (XVII) can be accounted for by the 1,4-addition of precisely this form of silylurea to benzoyl isocyanate[91,92]. The reaction mechanism evidently includes the formation of an unstable 1 : 1 adduct (XVIII) and its subsequent reactions via the following mechanism[91,92]:



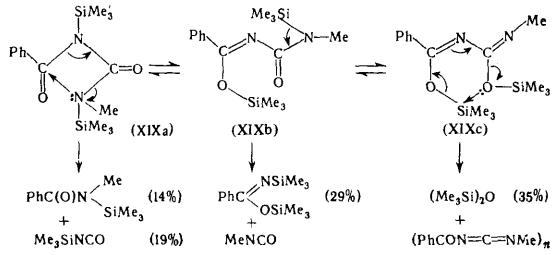
(XVIII) (XVI) (XVII)

In contrast to dialkyl-*N*-(trimethylsilyl)amines, heptamethyldisilazane $(Me_3Si)_2NMe$ forms with benzoyl isocyanate 1 : 1 (XIX) or 1:2 (XX) adducts depending on the reactant ratio[93]:

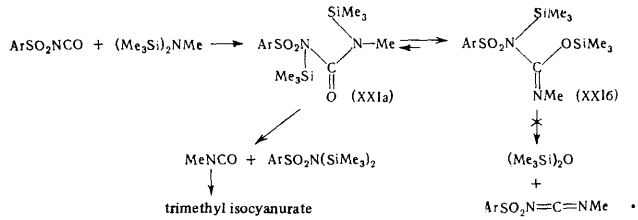


(XIX) (XX)

According to ^{1}H NMR data, the adduct (XIX) is a mixture of at least two isomers and the composition of the products formed on its pyrolysis indicates the possibility of the existence of three isomers of (XIX)[93]:



Reactions with sulphonyl isocyanates. Sulphonyl isocyanates react with aminosilanes (in proportions of 1 : 1) to give a quantitative yield of *N*-silyl-substituted sulphonated ureas, among which the main species is the carbonyl form (XXIa)[94]. This is confirmed by infrared spectroscopic and ^{1}H NMR data and also by the composition of the products of the pyrolysis of the compounds in which an organic isocyanate (or its trimer) and *NN*-bis(trimethylsilyl)sulphonamide are formed, in contrast to the pyrolysis of the analogous adducts of isocyanates and aminosilanes:

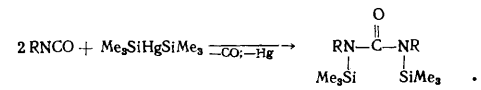


In conclusion of this section, one may note that, apart from the direct interaction of aminosilanes with isocyanates, *N*-silylureas are also formed in the reaction of aminosilanes with carboxylic acid azides[95]. At a low temperature in the presence of catalytic amounts of $AlCl_3$ or close to the decomposition temperature of the azide, this reaction proceeds as a double decomposition with formation of silyl azides and acid amides:

$$RC(O)N_3 + Me_3SiNR'R'' \rightarrow Me_3SiN_3 + RC(O)NR'R''$$

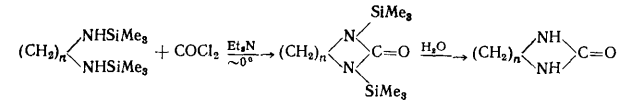
When this temperature is exceeded, the acid azide decomposes with liberation of the isocyanate, which then reacts further with the silylamine present to give a silylurea. In particular, high yields of trimethylsilyl-substituted derivatives of *N*-butyl-*N'*-phenyl- and *N*-benzyl-*N'*-phenylureas were obtained in this way (the position of the silyl residue in the ureas was not determined).

The interaction of isocyanates with bis(trimethylsilyl)-mercury in hexametapol yielded bissilylureas[96]:

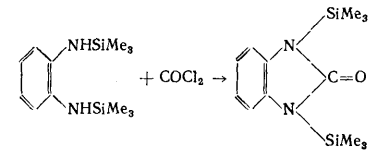


e. Other Methods of Synthesis

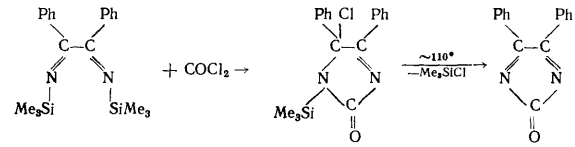
Birkofer et al.[38] showed in 1960 that cyclic derivatives of silylurea are formed in 60–75% yield in the reaction of phosgene with bissilyl-substituted tri- and tetra-methylenediamines in the presence of triethylamine. In the hydroxysis or methanolysis of these compounds organic derivatives of urea, which could not be synthesised by direct phosgenation of $\omega\omega'$-diamines, were obtained in quantitative yields:



Under the same conditions, *NN'*-bis(trimethylsilyl)-*o*-phenylenediamine reacts with $COCl_2$ to give *NN*-bis(trimethylsilyl)benzimidazol-2-one[38]:



while benzylbis(trimethylsilyl)imine is converted at −10°C into the thermally unstable silylimidazoline[97], which decomposes on heating to 4,5-diphenylimidazol-2-one:



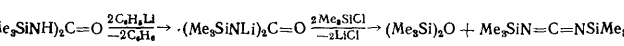
In contrast HMDS reacts with phosgene mainly according to the mechanism

$$6(Me_3Si)_2NH + 3COCl_2 \rightarrow 2(Me_3Si)_2NH + 5Me_3SiCl + 3Me_3SiNCO + NH_4Cl$$

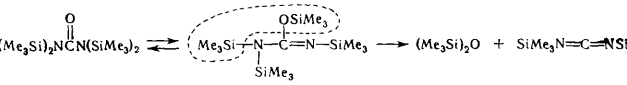
and not to give silyl-substituted ureas as might have been expected[18]. The interaction of metallated HMDS with $COCl_2$ also did not lead to the formation of the expected tetrasilylurea[18,98,99]. The stable bis(trimethylsilyl)carbodiimide and hexamethyldisiloxane were isolated as the main products of this reaction, the mechanism of which the authors were unable to elucidate:

$$2(Me_3Si)_2NNa + COCl_2 \rightarrow 2NaCl + (Me_3Si)_2O + Me_3SiN{=}C{=}NSiMe_3$$

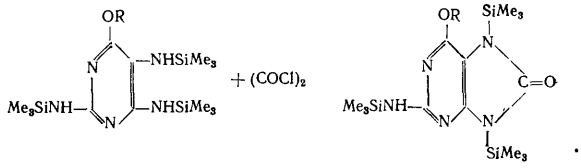
The attempts to obtain tetrasilylurea via the lithio-derivative of bis(trimethylsilyl)urea were also unsuccessful[98,99]. Despite the formation of lithium chloride, the same products were isolated from the reaction mixture:



Tetrasilylureas are nevertheless evidently formed as intermediates in these reactions, but, owing to their thermal instability, they decompose to the above compounds. Bearing in mind the tendency of *N*-silylureas (and silylamides in general) to undergo tautomerism and also the thermal instability of the compounds with the Si–N–C–X bond system (X = electronegative groups) observed previously[7,100], the following mechanism of the decomposition reaction appears to be most likely:



On treatment with oxalyl chloride, 2,4,5-tris(trimethylsilylamino)pyrimidines form compounds with a urea moiety in the ring system—silylpurines[101]:



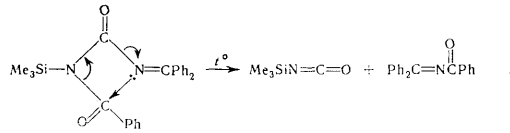
2. PHYSICAL PROPERTIES

Depending on the substituents at the silicon and nitrogen atoms, *N*-silylureas are liquid, oily, or crystalline substances, which are in most cases readily soluble in acetone, carbon tetrachloride, chloroform, ether, dioxan, and THF and more sparingly soluble in benzene, toluene, xylene, and petrol[18,41,53,66]. Their solubility in petroleum ether is as a rule low. Partly nitrogen-substituted derivatives, such as $Si(NHCONHPh)_4$ and $(OCN)_2Si(NHCONHPh)_2$, do not have distinct melting points and like urea are sparingly soluble in organic solvents.[41] Crystalline products sublime on heating *in vacuo*, and this can be used for their purification[18,41,53].

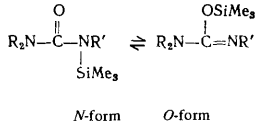
The thermal stability of *N*-silylureas was not specially studied, but it evidently varies within wide limits and depends mainly on the structure and the presence of secondary impurities. Thus the compounds $Me_3SiNHC(O)NPh_2$ and $Me_2Si(NHCONPh_2)_2$ decompose fully at about 250°C to isocyanatosilane and diphenylamine. This reaction was proposed for the synthesis of isocyanatosilanes[6]. On heating urea with HMDS at 90–110°C in the presence of $(NH_4)_2SO_4$, Me_3SiNCO is formed in a yield in excess of 90%, which is also evidence for the thermal instability of the intermediate silylurea.

On the other hand, the compound $Me_3SiNHC(O)NEt_2$ is stable in the absence of moisture up to 300°C and $Me_3SiNHC(O)NBu_2$ and $Me_3SiNHC(O)NMe_2$ merely sublime on heating to 220°C.[41] On the other hand, according to the data of other workers[18], in the presence of HMDS the complete decomposition of the latter compound to Me_3SiNCO and Me_2NH occurs already at the boiling point of HMDS (about 126°C).

Tetrakis(trialkylsilyl)ureas could not be obtained, probably owing to their thermal instability[98,99]. The decomposition of *N*-acyl-*N*-silylureas on heating proceeds with formation of isocyanatosilane and *N*-(diphenylmethylene)benzamide[75]:



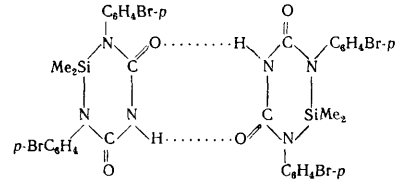
By analogy with *N*-trimethylsilylamides of carboxylic acids, which are capable of amide–isoamide tautomerism involving the Me_3Si group[30], Klebe et al.[53] suggested the possibility of the same type of tautomerism also for silicon-containing ureas:



N-form *O*-form

Comparison of the infrared and ultraviolet spectra of the compounds[11,18,41,52,56,61–63,66,70,102] with those of model molecules does not, however, allow unambiguous conclusions in this respect. All the compounds have absorption bands in the range 1500–1700 cm^{-1}, characteristic of secondary and tertiary amides. The study of a number of *N*-organosilyl-*N'*-phenylureas[70] showed that in the solid state they apparently contain only hydrogen-bonded N–H groups, while in solution there exist also associated N–H groups, to which the 3413 and 3517 cm^{-1} bands correspond. The 3413 cm^{-1} band was assigned to the phenyl–NH group and the 3517 cm^{-1} band to the silyl–NH group. The 3280, 3323, 3324, 3341, and 3349 cm^{-1} bands, observed in the spectra of suspensions of these compounds, were assigned respectively to bound phenyl–NH and silyl–NH groups. The comparatively high stretching vibration wavenumbers of the free NH group and their appreciable displacement on passing from solutions to suspensions (from 176 to 194 cm^{-1} for various substituents at the silicon atom), demonstrates the amphoteric nature of the silyl–NH group and the greater mobility of its proton compared with that of the phenyl–NH group (the corresponding shift is 133 cm^{-1}). One of the explanations of this finding involves the participation of the lone electron pair of the nitrogen atom in the formation of a bond with silicon and hydrogen, the degree of involvement of this pair depending on the nature and strength of the intermolecular interaction. In the formation of a hydrogen bond the lone electron pair is probably located at the silicon–nitrogen bond[70].

According to X-ray diffraction analysis, the molecules of 2,6-di(*p*-bromophenyl)-1,1-dimethyl-1-sila-2,4,6-triazacyclohexanedione (the product of the reaction of the *p*-bromophenyl isocyanate with HMDS) are dimerised in the crystal by hydrogen bonding[79]:



The spectra of silylureas obtained by the interaction of Et_2NSiMe_3 or silazanes with phenyl isocyanate do not contain the intense band due to the stretching vibrations of the silicon–nitrogen band, which is observed in the spectra of the initial compounds at 925 and in the range 900–950 cm^{-1} respectively. Its disappearance is explained by the fact that the corresponding vibration in silylureas is no longer characteristic and is not observed in the same part of the spectrum[63]. Other workers assign the bands at 850, 848, and 840 cm^{-1} to the ν_{as} vibrations of the Si–N bond in $(Me_3SiNH)_2CO$, $(Me_3Si)_2NC(O)NHPh$, and $Si(NHCONH_2)_4$ respectively[18].

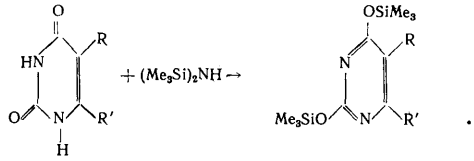
The infrared spectrum of tetraureidosilane $Si(NHCONH_2)_4$ has an absorption band at 2175 cm^{-1}, which is the most intense in the sublimate formed on heating the urea *in vacuo* at 160°C. It is assigned to the ν_{as} stretching vibrations of the N=C=N group, the formation of the latter being explained by partial decomposition via the reaction[18]

$$Si(NHCONH_2)_4 \rightarrow 4H_2O + Si(N{=}C{=}NH)_4 .$$

The ^1H NMR spectra of a number of silylureas have been published[52,66,73,75,89,92–94]. The study of the nature of the Me_3Si signal as a function of temperature showed that in the case of a number of silylureas, for example $Me_3SiN(Me)C(O)NMe_2$ and $PhSO_2N(SiMe_3)C(O)NMe_2$, the

signal due to the protons of this group does not split at low temperatures[92]. This is evidence for the absence of appreciable tautomerism or for the presence of a mixture of *O*- and *N*-forms with their very rapid interconversion even at low temperatures. On the other hand, the signal for other compounds, for example $PhC(O)N(SiMe_3)C(O)NR_2$ [76,92] and $Ph_2C{=}NC(O)N(SiMe_3)R$ [75] splits into two at temperatures below −43°C, which has been interpreted as supporting the 1,3-transfer of the Me_3Si group, i.e. the presence of the *O*-silyl form of ureas (amide–isoamide tautomerism). As already mentioned above, the formation of the isoamide form is also indicated by a number of chemical reactions of silylureas[75,76,92].

The presence of only the *O*-form has been established for certain cyclic silylureas. For example, silylation of uracil derivatives with HMDS results in the formation of silyl derivatives which have the structure of siloxypyrimidines and not *N*-silyluracils[23,103]:



3. CHEMICAL PROPERTIES

The majority of silylureas are unstable with respect to hydrolysis[18,41,52,55,57,61–63,66,68,69,73,95,104] and readily deliquesce in moist air[66]. They are hydrolysed with dissociation of the Si–N bond and the formation of organosilanols (or organosiloxanes) and organic urea derivatives[41,68,73,75,95]:

$$2\,Me_3SiNHC(O)NR_2 + H_2O \rightarrow (Me_3Si)_2O + 2H_2NC(O)NR_2 \quad .$$

On the other hand, in contrast to asymmetric ureas, *NN'*-bis(trimethylsilyl)urea is hydrolysed by water with considerable difficulty[18]. According to the authors, electron density is in this case redistributed in the direction which lowers the double bond character of the linkage between the Si and N bonds and this ultimately reduces the susceptibility of the silicon atom to nucleophilic attack. Incidentally, one cannot rule out the possibility that hydrolysis is slow because the reaction takes place in a heterogeneous medium owing to the sparing solubility of the silylurea in water.

N-Silylureas, particularly aromatic derivatives, are powerful silylating agents, like carboxylic acid silylamides[22,25,26,36]. Their reactions with amines and hydroxy-compounds are rapid even at room temperatures and lead to the quantitative formation of the corresponding silyl derivatives with removal (or in some cases without removal) of one of the components of the equilibrium mixture. For example, $Me_3SiN(Ph)CONHPh$ and *NN'*-dimethylurea are completely converted after 1 min at 20°C[22]:

$$Me_3SiN(Ph)CONHPh + MeNHCONHMe \rightarrow Me_3SiN(Me)CONHMe + PhNHCONHPh \quad .$$

Experiments with compounds containing an active hydrogen atom at a carbon atom (acetylacetone, nitromethane, and malononitrile) showed that these too are capable of undergoing the silyl–proton exchange with silylureas[22].

Alcoholysis

When silylureas are treated with an alcohol, solvolysis takes place with formation of alkoxysilanes and organic urea derivatives[25,88,89,105], for example:

$$Me_3SiNHC(O)NMe_2 + EtOH \rightarrow Me_3SiOEt + H_2NC(O)NMe_2 \quad .$$

The methanolysis of optically active silylureas and biuret is accompanied, with rare exceptions[74], by the reversal of the configuration at the silicon atom[73], which indicates an S_N2 mechanism for this reaction:

$$(+)\text{-}R_3Si^*NCONHMe + MeOH \rightarrow (+)\text{-}R_3Si^*OMe + PhNHCONHMe \quad ,$$

$$(-)\text{-}R_3Si^*NCONCONHPh + MeOH \rightarrow (+)\text{-}R_3Si^*OMe + PhNHCONCONHPh \quad ,$$

where $R_3Si^* = (\alpha\text{-}C_{10}H_7)PhMeSi^*$.

Aminolysis

The compounds readily enter into a reversible reaction with amines, which is fully displaced to the right owing to the sparing solubility of the resulting urea or biuret derivatives, and, like alcoholysis, is accompanied by the reversal of the configuration[73].

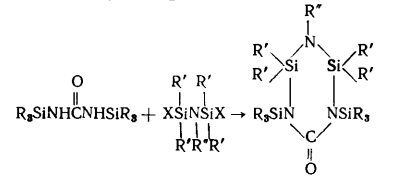
$$(+)\text{-}R_3Si^*NCONHMe + Me_2NH \rightleftarrows (+)\text{-}R_3Si^*NMe_2 + PhNHCONHMe \quad .$$

Silylureas react with acids according to the mechanism[74]:

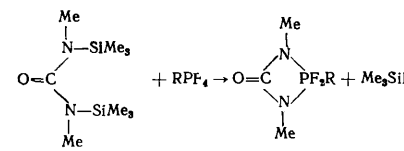
$$R_3SiNC(O)NMe_2 + PhCOOH \rightarrow R_3SiOC(O)Ph + PhNHC(O)NMe_2 \quad .$$

Kaufmann et al.[74] showed that, in contrast to silylamines and *N*-silylthioureas, the Si–N bond in silylureas is not cleaved under the influence of *p*-nitrobenzoyl chloride.

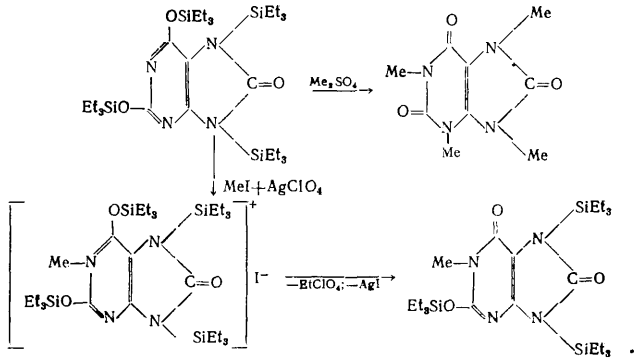
1,3-Dihalogenosilazanes react with *NN*-bis(trimethylsilyl)ureas to form cyclic products[106]:



When acted upon by fluorophosphoranes, asymmetric disilylureas form fluorophosphadiazetidinediones with cleavage of the Si–N bond[107]



Silyl derivatives of uric acid react with dialkyl sulphates or methyl iodide to form alkyl derivatives of uric acid[101]:



4. APPLICATIONS

The interest in silylureas is due to their ability to form compositions which are self-hardening at the normal temperature, their high silylating activity, and many other valuable properties.

According to patent data, monomeric *N*-triorganosilylureas are effective agents for the treatment of fabrics, paper, leather, and non-fibrous materials (for example, cellophane) in order to make them hydrophobic and creaseless, to reduce their brittleness, and to improve other characteristics[5,17]. *N*-Silylureas can be used in the synthesis of plastics[54], lubricating oils, and hydraulic liquids[36,55], for the stabilisation of poly(vinyl chloride)[42], as vulcanisers for the cold-hardening of polysiloxanes[108], and for other purposes[109,110]. Some of these compounds exhibit pharmacological and pesticidal properties[17,36,54,65,-111,112]. Silylureas with unsaturated groups in the molecule have been patented in connection with the synthesis of block copolymers and the vulcanisation of polyorganosiloxane elastomers[72].

The polysilylureas formed when isocyanatosilanes react with polyamines can be thermoplastic or thermoreactive, depending on the type of the initial reactants; they have been suggested for the formation of moulded articles, laminated materials based on fibreglass, and for many other purposes[43,113-115]. Polysilylurea films have a high breakdown voltage and tensile strength[83,85].

Polysilylureas obtained from organic polyisocyanates and silylamines have many valuable properties. Polymeric materials of this kind can be used to synthesise elastomers[116], fibres, and films[117] and for other purposes[87,118]. The susceptibility of the Si–N bond to hydrolysis does not preclude their employment since, on being acted upon by atmospheric moisture, the film is only partly hydrolysed on the surface and the liberated siloxane plasticises the material.

The polyureidosilazanes, obtained when linear or cyclic silazanes are treated with organic polyisocyanates, adhere effectively to metals, glass, and rubber, are resistant to the action of water, organic solvents, acids, and alkalis, and have satisfactory dielectric and other properties[78,86,119].

Monomeric and polymeric silylbiurets[64,65,84,120] have been patented as antifoaming and anti-ageing agents, as agents accelerating vulcanisation, and as plasticisers and herbicides.

III. SILYLISOUREAS

Silylisoureas were obtained for the first time in 1968 by the reaction of cyanic acid esters with aminosilanes or silazanes[121,122]. This reaction proceeds mainly similarly to the reaction of aminosilanes with isocyanates, i.e. with cleavage of the Si–N bond and addition to the multiple bond of the cyanate. However, in contrast to isocyanates, cyanic acid esters can also enter into an exchange reaction involving the Si–N bond of the aminosilane similar to the Brown cleavage reaction. Dialkylaminosilanes are known[123] to enter into a similar reaction with bromocyanogen, forming bromosilane and dialkylcyanamide. When there is a possibility of competing reactions involving the Si–N and N–H bonds, as happens in the case of secondary aminosilanes, the Si–N bond is cleaved first. The interaction of cyanates with various types of aminosilanes is to some extent specific.

The reaction of cyanic acid esters with dialkyl-*N*-trimethylsilylamines in 1:1 proportions results in the quantitative yield of *NN*-dialkyl-*N'*-trimethylsilylisoureas[121]:

$$ROC{\equiv}N + R'_2NSiMe_3 \rightarrow ROC(=NSiMe_3)NR'_2 ,$$

where R = aryl and R′ = alkyl. The same compounds can be obtained by the silylation of *NN*-dialkylisoureas with chlorotrimethylsilane[121].

When the resulting isourea is acted upon further by the cyanate, the products are 2-dialkylamino-4,6-diaryloxy-*s*-triazines and aryl trimethylsilyl ethers:

$$ROC(=NSiMe_3)NR'_2 + 2ROC{\equiv}N \rightarrow \text{2-dialkylamino-4,6-diaryloxy-}s\text{-triazine} + Me_3SiOR .$$

Thus, in contrast to isocyanates, cyanic acid esters do not form 1:2 adducts with dialkyl-*N*-trimethylsilylamines, since the first stage of this reaction is an addition process and the second is a process of the type of the Brown reaction.

The reaction of alkyl-*N*-trimethylsilylamines with aryl cyanates in proportions of 1:1 results in the initial formation of *N*-alkyl-*O*-aryl-*N'*-trimethylsilylisourea (possibly in a mixture with its isomeric form). However, these compounds cannot be isolated, since under the influence of the cyanate they are immediately converted into *N*-alkyl-*O*-aryl-*N'*-cyanoisoureas with elimination of the Me_3Si group:

$$RNHSiMe_3 + ArOCN \rightarrow \left[ArO{-}C(=NR){-}NHSiMe_3 \rightleftarrows ArO{-}C(NHR){=}NSiMe_3 \right] \xrightarrow{ArOCN} ArO{-}C(NHR){=}N{-}CN + ArOSiMe_3 .$$

In addition, phenol, carbodiimide, and polymerisation products of the latter are formed in small amounts.

The reaction with HMDS proceeds similarly. In this case too it was impossible to isolate the 1:1 adduct, which is converted under the influence of ArOCN into *O*-aryl-*N*-cyano-*N'*-trimethylsilylisourea. At an elevated temperature a silylated cyanoguanidine is formed in addition. The reaction can be represented as follows:

$$ArOCN + (Me_3Si)_2NH \rightarrow \left[ArO{-}C(=NSiMe_3){-}NHSiMe_3 \right] \xrightarrow[ArOSiMe_3]{ArOCN} \left[ArO{-}C(NHSiMe_3){=}N{-}C{\equiv}N \right] \rightleftarrows \left[ArO{-}C(=NSiMe_3){-}NH{-}C{\equiv}N \right] \rightleftarrows \left[ArO{-}C(=NSiMe_3){-}N{=}C{=}NH \right] .$$

On the other hand, the reaction of methyl-*NN*-bis(trimethylsilyl)amine with ArOCN (in proportions of 1 : 1 or 1 : 2) is of the double addition type with formation of the 1 : 2 adduct—the diaryl ester of N^2-methylimino-N^1N^3-bis(trimethylsilyl)carbamic acid. Only in the presence of an up to sixfold excess of the cyanate are the Me_3Si groups exchanged for CN with formation of the diaryl ester of N^1N^3-dicyano-N^2-methyliminocarbamic acid, which tends to polymerise:

$$(Me_3Si)_2NMe + 2PhOCN \rightarrow \begin{matrix} PhO-C=NSiMe_3 \\ | \\ Me-N \\ | \\ PhO-C=NSiMe_3 \end{matrix} \xrightarrow[-PhOSiMe_3]{+PhOCN} \begin{matrix} PhO-C=N-CN \\ | \\ Me-N \\ | \\ PhO-C=N-CN \end{matrix} .$$

Silylisoureas are colourless viscous oils, which can be distilled without decomposition in a high vacuum. Their infrared spectra contain intense bands in the ranges 1745–1755 and 1685–1698 cm^{-1}, which are characteristic of the stretching vibrations of the double bond of the silylated imido-group $\diagdown C{=}NSi \diagup$.

At high temperatures (for example under the conditions of gas-chromatographic analysis) the silylisoureas decompose via the mechanism

$$RO-\underset{\underset{NR'_2}{|}}{C}=N-SiMe_3 \xrightarrow{t^\circ} ROSiMe_3 + R'_2N-C\equiv N .$$

On treatment with alcohols or on prolonged standing in air, they are desilylated to organic isoureas. The reaction with acid chlorides also proceeds with the cleavage of the Si–N bond and the formation of acyl isoureas and chlorosilanes[121].

IV. CARBOFUNCTIONAL ORGANOSILICON DERIVATIVES OF UREA

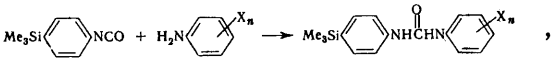
1. METHODS OF SYNTHESIS

Silicon-containing derivatives in which the urea moiety and the silicon atoms are separated by a group of atoms have been less thoroughly investigated. The majority of the methods for their preparation reduce mainly to the familiar procedures of organic chemistry for the synthesis of alkyl (or aryl)-substituted urea derivatives (isocyanate condensation transamination, and other reactions) and are based on the employment as the starting materials of the corresponding isocyanates and amines or compounds containing an amino-group.

a. Isocyanate Condensation Reactions

Two versions of isocyanate condensation via a combination of organic and organosilicon starting materials are possible: (1) the interaction of carbofunctional organosilicon isocyanates with organic or organosilicon amines and (2) the interaction of organic isocyanates with carbofunctional silicon-containing amines.

Until 1959, the first reaction was illustrated by only one example[124]:



where X = Cl, MeO, EtO, or H and n = 1 or 2.

A wide variety of both mono- and di-silyl-substituted ureas became available recently after the development of convenient methods for the preparation of carbofunctional organosilicon isocyanates[125]. In particular, the first and simplest representatives of aliphatic silicon-containing ureas $R_3Si(CH_2)_nNHCONH_2$ [7,126–130] and also ureas with a disiloxane bond of the type $[H_2NCONH(CH_2)_nSiMe_2]_2O$ [6,7] were obtained recently from these compounds.

Carbofunctional organosilicon isocyanates as a rule react exothermically with amines to form the corresponding urea derivatives in virtually quantitative yields [6,7,126,127,130–136]:

$$R_3Si(CH_2)_nNCO + Bu_2NH \rightarrow R_3Si(CH_2)_nNHC(=O)NBu_2 ,$$

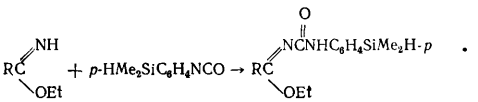
where R = Me, Et, or Ph and n = 1 or 3.

ω-Isocyanatoalkylsilanes with an NCO group in the γ-position are more reactive than α-isocyanatoalkylsilanes[130,135].

When isocyanates react with hydrazine and its derivatives, silylsemicarbazides are formed[134,137,138]:

$$[OCN(CH_2)_3SiMe_2]_2O + R_2NNH_2 \rightarrow [R_2NNHC(=O)NH(CH_2)_3SiMe_2]_2O,$$

and the reaction with aminoethers gives a high yield of carbamidoiminoethers[139]:



Organosilicon isocyanates react just as easily with acid hydrazides to form the compounds $R_3Si(CH_2)_n$. .$NHCONHNHCOAr$.[130]

The interaction with acid amides is more difficult[130]. For example, benzamide and sulphonamides form the substituted ureas $R_3Si(CH_2)_nNHCONHCOPh$ and $R_3Si(CH_2)_n$. .$NHCONHSO_2Ar$ only after prolonged heating with isocyanate in dimethylformamide (DMF) in the presence of triethylamine as the catalyst.

Symmetrical silicon-containing ureas have been obtained on heating carbofunctional organosilicon isocyanates with water in DMF[140]:

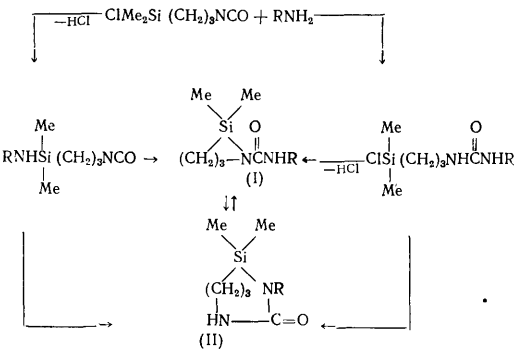
$$R_3Si(CH_2)_nNCO + H_2O \rightarrow [R_3Si(CH_2)_nNHCOOH] \xrightarrow{-CO_2} R_3Si(CH_2)_nNH_2 \xrightarrow{R_3Si(CH_2)_nNCO} \rightarrow R_3Si(CH_2)_nNHC(=O)NH(CH_2)_nSiR_3,$$

where R = Me, Et, or Pr and n = 1 or 3. In the presence of an excess of water an organosilicon amine is formed in this reaction.

In contrast to the reactions with amines and alcohols, where α-isocyanatomethylsilanes have a reduced reactivity compared with γ-isocyanatoalkylsilanes, in the reaction with water these compounds have virtually the same reactivities[140]. Evidently the overall electropositive effect of the R_3SiCH_2 group in α-isocyanates is manifested in two ways: on the one hand, the electrophilicity of the carbonyl carbon atom is reduced and the rate of reaction of the isocyanate with water is diminished and, on the other, the basicity of the resulting amine is enhanced, as a result of which the rate of the secondary reaction (the reaction with the isocyanate) rises.

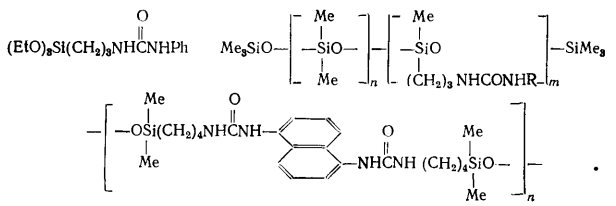
Isocyanates with other reactive groups or atoms at the silicon atom can interact with amines via these groups too. Thus the reaction of $ClMe_2Si(CH_2)_3NCO$ with an excess of a

primary amine results in the formation of 1-alkylcarbamido-1-aza-2-silacyclopentanes (I), which are in a state of tautomeric equilibrium with 1,3-diaza-4-silacycloheptan-2-ones (II)[7,141]:

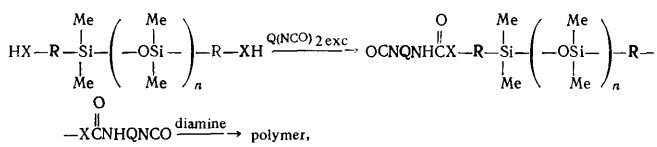


The reactions of organosilicon diisocyanates with diamines, hydrazines, and dihydrazides yielded respectively polysilylureas[142-144], polysilylureylenes[142,145], and polyacylsemicarbazides[146,147].

The reaction of organic isocyanates with carbofunctional organosilicon amines has been little investigated, although it has been shown for the synthesis of monomeric, oligomeric, and polymeric ureas that it is of a general type[148-151]. In particular, compounds having the following formulae have been obtained:



A number of oligomeric and polymeric compounds containing in the chain alternating siloxane, urethane, and urea units have also been synthesised by the isocyanate condensation reaction using organic diisocyanates[150,151]:



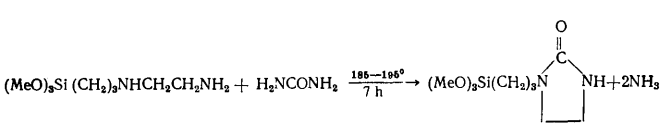
where R and Q = alkylene or arylene and X = O or NH.

b. Transamination Reactions

Silicon-containing ureas are formed in satisfactory yields on prolonged heating of high-boiling organosilicon amines with the urea[152]:

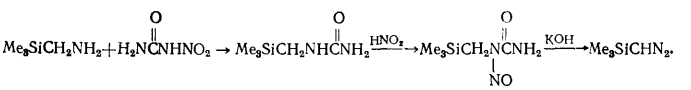
$$2\,(EtO)_3Si\,(CH_2)_3NH_2 + H_2NCONH_2 \xrightarrow[7.5\ h]{185^\circ} [(EtO)_3Si\,(CH_2)_3NH]_2CO + 2NH_3.$$

When organosilicon diamines are used in the reaction, cyclic silylureas are formed[153,154]:



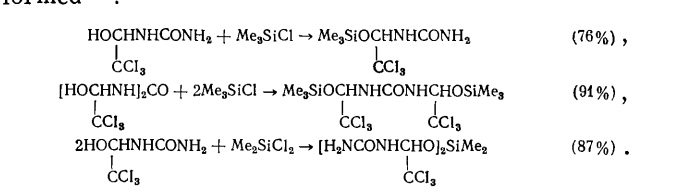
Hydrolysis of such cyclic or linear compounds with alkoxy-groups at the silicon atom leads to the formation of polysiloxanes with urea units in the side chain. Copolymers of these compounds with silanes and siloxanes containing hydrolysable groups at the silicon atom have also been obtained[153,154].

Using the transamination reaction, Seyferth and coworkers[155,156] synthesised *N*-nitroso-*N*-trimethylsilylurea, which is a convenient starting material for the synthesis of the unusually stable trimethylsilyldiazomethane. The synthesis was carried out in accordance with a scheme similar to that used in the synthesis of a diazomethane from *N*-methyl-*N*-nitrosourea:



c. Silylation of Urea Derivatives

When the products of the condensation of chloral with urea are acted upon by chlorosilanes in the presence of an excess of pyridine, high yields of siloxyureas are formed[157]:



Similar derivatives were obtained by treating mono- and di-(hydroxymethyl)ureas with chlorotrimethylsilane and triethylamine[104]. A study of the reaction of mono(hydroxymethyl)urea with Me_3SiCl has shown that, even for an equimolar reactant ratio, Me_3SiCl reacts with the hydrogen atoms of both OH and NH_2 groups:

$$H_2NCONHCH_2OH + Me_3SiCl \xrightarrow[-Et_3N\cdot HCl]{Et_3N} Me_3SiNHCONHCH_2OSiMe_3 \qquad (39\%).$$

When Me_3SiCl is allowed to react with di(hydroxymethyl)-urea, only the hydrogen atoms in the hydroxy-groups are substituted:

$$O{=}C\,(NHCH_2OH)_2 + 2Me_3SiCl \xrightarrow[-Et_3N\cdot HCl]{Et_3N} O{=}C\,(NHCH_2OSiMe_3)_2 \qquad (44\%).$$

Silylation of the hydroxymethyl groups in *NN'*-di(hydroxymethyl)urea proceeds readily also when the latter is acted upon by HMDS, *N*-trimethylsilylacetamide, *NO*-bis(trimethylsilyl)acetamide, diethyl-*N*-trimethylsilylamine, and dimethyl-*N*-trimethylsilylamine at about 35°C in acetone, pyridine, or ethyl acetate, dialkyl-*N*-trimethylsilylamines being the most effective silylating agents[158]. This reaction has been used to silylate the products of the condensation of urea with formaldehyde in order to decompose intramolecular and intermolecular hydrogen bonds in aminoplastics, which leads to the formation of products soluble in organic solvents to which gel-chromatographic research techniques are applicable[158].

According to Kreshkov et al.,[159] the hydroxy-groups in urea-formaldehyde resins can react with alkoxysilanes, probably via the following mechanism:

By combining urea-formaldehyde resins with polyethoxypolysiloxanes, silicon-modified polymers were obtained using this procedure[159].

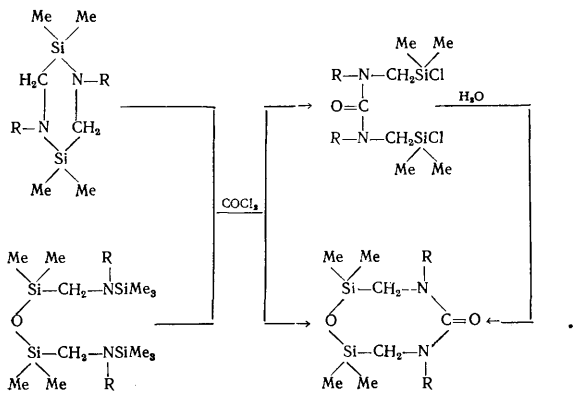
d. Other Reactions

Montgomery[160,161] synthesised symmetrical silicon-containing derivatives by heating aminoalkylsilanes with carbonyl sulphide in an autoclave:

$$PhMe_2SiCH_2NH_2 + COS \xrightarrow[4\ h]{100^\circ;\ 1\ atm} [PhMe_2SiCH_2NH]_2CO + H_2S\ ,$$

$$Me_3SiOSi(Me)_2CH_2NH_2 + COS \xrightarrow{100^\circ;\ 8.6\ atm} [Me_3SiOSi(Me)_2CH_2NH]_2CO + H_2S\ .$$

Linear and cyclic compounds were obtained by treating piperazine rings with phosgene and by synthesis from *N*-silylated α-diamines of the disiloxane series[162]:



When urea is acylated with the chlorides of organosilicon acids, the products are acylureas with a silicon atom in the acyl residue[163,164].

A number of other methods known only in organic chemistry can be used to synthesise organosilicon ureas. In particular, ureas are formed when carbofunctional organosilicon amines are treated with carbamoyl chlorides[6,7]:

$$Me_3SiCH_2NH_2 + Ph_2NC(O)Cl \xrightarrow[-Et_3N\cdot HCl]{Et_3N} Me_3SiCH_2NHC(O)NPh_2 \qquad (62\%)$$

and on oxidising the corresponding amines with lead tetraacetate in the presence of an amine[6,7]:

$$Me_2EtSi(CH_2)_3CNH_2 \xrightarrow[DMF]{Pb(OAc)_4} [EtMe_2Si(CH_2)_3NCO] \xrightarrow{AllNH_2} Me_2EtSi(CH_2)_3NHC(O)NHAll.$$

A number of cyclic urea analogues having the structure of uretidinediones were obtained by the reaction of halogenoalkylsilanes with metal cyanates in DMF. The formation of these compounds is due to the dimerisation of the isocyanates, which are the primary reaction products, under the influence of the cyanate salt[165-167]:

$$R'R_2Si(CH_2)_nCl \xrightarrow[-MCl]{MOCN} [R'R_2Si(CH_2)_nNCO] \rightarrow R'R_2Si(CH_2)_nN(C(O))_2N(CH_2)_nSiR_2R'\ ,$$

where R and R′ = Me, Et, or Ph, n = 1 or 3, and M = K or Na.

When bishalogenoalkylsilanes are used in this reaction, the analogous oligomeric compounds are formed:

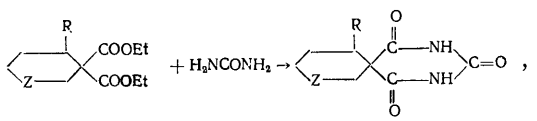
$$Cl(CH_2)_nSiR_2O[SiR_2(CH_2)_nCl] + KOCN \rightarrow OCN(CH_2)_nSiR_2O[SiR_2(CH_2)_nNCO] +$$

$$+ OCN\left[-(CH_2)_nSiR_2O[SiR_2(CH_2)_nN(C(O))_2N-]\right]_m(CH_2)_nSiR_2O[SiR_2(CH_2)_nNCO.$$

Silicon-containing uretidinediones were obtained in low yields also by treating carbofunctional organosilicon amines with phosgene[7]. Finally, silyl-substituted barbiturates were obtained by the condensation of urea with organosilyl malonates[168,169]:

$$Me_3Si-R-C(R')(COOEt)_2 + H_2NCONH_2 \rightarrow Me_3Si-R-C(R')(C(O)NH)_2C(O)\ ,$$

where R = $-CH_2-$ and R′ = H, Me, or allyl[168] or R = $-C_6H_4-$ and R′ = H or Et[169], and with spirobarbiturates[170]:



where Z = $SiMe_2$ or CH_2SiMe_2 and R = H, Me, or Et.

2. PROPERTIES

Carbofunctional organosilicon ureas are colourless viscous liquids or crystalline substances. Some decompose appreciably on vacuum distillation[171]. They are readily soluble in benzene, acetone, and DMF and are insoluble in water and petroleum ether[130,171].

Silicon-containing acylureas and semicarbazides are crystalline substances soluble in DMF and alcohol and sparingly soluble or insoluble in water, benzene, and carbon tetrachloride[130].

The infrared spectroscopic data for silylureas[6,7,130-132,133,141,142,172], silylsemicarbazides[137], and silylpolyacylsemicarbazides[146] agree well with the amide structure of these compounds. The characteristic absorption bands of the C=O group (amide band I) in the infrared spectra of asymmetric ureas of the type $R_3Si(CH_2)_nNHCONR_2$ are in the region of 1630 cm^{-1}.[130] The analogous bands in the spectra of polysilylureas are at 1650 cm^{-1}.[132]

An appreciable decrease of the carbonyl absorption wavenumber (1690 cm^{-1}) has been observed for uretidinediones (cyclic compounds) $R_3Si(CH_2)_nNC(O)N(CO)(CH_2)_n$. .$SiR_3$ compared with compounds of analogous structure but without silicon (1780–1790 cm^{-1}). A similar decrease of the C=O vibration wavenumber is known to occur in the spectra of organosilicon ketones $R_3Si(CH_2)_nC(O)Me$. Evidently, in this case there is an appreciable decrease of the amount of double bond character of the linkage joining the carbonyl group owing to the intramolecular coordination of its oxygen atom to silicon[165]. The bond formed is fairly stable, as shown by the constancy of the extinction coefficient of the C=O band when the concentration of the substance is reduced from 0.1 to 0.0001 M.

NMR data for a number of silylureas have been published[7,141].

When organosilicon ureas are pyrolysed, an isocyanate and an amine are formed, as from their hydrocarbon analogues[6]:

$$Me_3SiCH_2NHC(=O)NPh_2 \xrightleftharpoons{250\div300^\circ} Me_3SiCH_2NCO\,(70\%) + Ph_2NH.$$

3. APPLICATIONS

Carbofunctional organosilicon ureas are of interest primarily for the preparation of modified polymeric materials. The study of various types of polymers (polyamides, polyimides, etc.) has shown[173] that the introduction of, for example, polysiloxane units into the organic polymeric chain in an amount of 3–5% entails a number of significant changes in the properties (a decrease of the yield temperature, an improvement in solubility and dielectric parameters) and makes polymeric materials hydrophobic and resistant to hydrolysis. When a large number of siloxane units (from 15 to 20%) are introduced, there is in addition an appreciable improvement in thermal stability.

The foregoing applies equally to carbofunctional organosilicon materials in which the organic and organosilicon fragments are linked chemically. Polymeric materials of this kind have been proposed for the preparation of coatings, resins for laminated plastics, stable water-repellent impregnation for cotton and paper fabrics[152,153], and self-vulcanising rubbers[174]. Monomeric and polymeric silylureas can be used as adhesives[152–154,175–177], antifoaming agents[160,161], auxiliary substances in the synthesis of glass fibre-reinforced plastics[135,178,179], surface-active substances[149,175,176,180], hardening agents for epoxy-resins[181], and other purposes[149,151–154,178,180,182–187]. Some of these compounds exhibit physiological activity[163,164,168–170,188].

Silicon-carbamide polymeric materials, obtained by the copolymerisation of urea-formaldehyde prepolymers with organosilicon polymers or oligomers[159,189], have been proposed for the preparation of varnish films, adhesives, cast articles, and laminated plastics with better dielectric parameters and improved thermal stability and water resistance compared with the usual urea-formaldehyde materials. Silyl ethers of hydroxymethyl derivatives of urea have been recommended for the preparation of rubbers which undergo self-cross-linking under the influence of moisture[190,191] and as intermediates in the preparation of medicines, textiles, and resins[192].

The use of compositions of monomeric or polymeric organic urea derivatives with silicon-containing compounds (components not linked chemically) is also a promising application[193–225]. For example, the introduction of 0.05–5% of urea, diphenylurea, or tolylurea into a vulcanisate improves the thermal stability of silicon elastomers[203]. The compositions are used to treat textiles in order to make them hydrophobic and crease-resistant[195,219,221,223,225], to improve the water resistance of aminoplastics[208], to bind polyurethanes to the support[213], as coatings[220,222], adhesives[215], lubricants[214,218], and binders for articles made of fibreglass[140], and for many other purposes.

Studies on the use of organosilicon products as auxiliary substances in the manufacture of various urea-based materials are also noteworthy[201,206,226]. Urea and its derivatives can be used in their turn as auxiliary products in the preparation of silicon-containing compounds, for example as ligands which reduce the activity of platinum catalysts in the addition of hydropolysiloxanes to olefinic silicones[227] and as solvents in the reduction of halogenosilicones with sodium hydride[228–230].

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Microbiological Degradation of Lignin

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The problems of the microbiological degradation of lignin, closely related to the solution of a number of important theoretical and practical problems, have been continually attracting attention in recent years. The most recent studies in this field are analysed in the present review. Particular attention has been devoted to a critical examination of hypotheses about the possible pathways in the microbiological degradation of lignin.
The present review is the first attempt in the Soviet scientific literature at a survey of data concerning the problem of the microbiological degradation of lignin.
The bibliography includes 151 references.

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1. INTRODUCTION

The microbiological degradation of plant materials, an important component of which is lignin, plays a significant role in the carbon turnover in nature. Studies on the degradation of lignin as a result of the activity of micro-organisms [1-14], which to a large extent differs from the degradation of other plant components, have widely developed in the last 10–15 years. These investigations are closely related to studies in a number of important fields, among which the following should be mentioned: (1) humus formation and the problem of soil fertility (see the relevant reviews [12,15-17]); (2) the formation of peat and coal; (3) the conservation of wood during storage (see the review of Cartwright and Findlay [18]); (4) the possibility of employing wood infected by fungii; (5) the metabolic transformations of plants in man and animals; (6) the use of the fungal mycelia to accumulate protein products; (7) delignification of plant raw materials in order to develop rational methods for the preparation of cellulose; (8) decontamination of natural waters by the removal of lignin-containing waste (see the relevant reviews [19,20]).

There is no need to stress the great theoretical and practical importance of the above studies. Furthermore, recent studies on the microbiological degradation of lignin yielded valuable information about its structure, which makes it possible to treat microbiological activity as one of the promising methods for the investigation of lignin.

Despite the importance of these studies, in the latest monograph on the chemistry of lignin [21] unjustifiably little attention was devoted to problems of its microbiological degradation. Furthermore, there are no reviews in the Soviet chemical literature on this field.

In view of the large amount and great variety of available data, it is impossible to consider here all the above aspects of the microbiological degradation of lignin. Attention will be concentrated below on studies which yielded information about the structure of natural lignin, i.e. lignin isolated from plant tissue.

II. WOOD DECOMPOSING FUNGI

Since the aims of the present review are restricted to the analysis of the results of studies on the microbiological degradation of lignin important for the determination of its structure, among the different biological agents causing decomposition of lignin (wood-decomposing fungi, soil and water micro-organisms, intestinal bacteria) only wood-decomposing fungi will be considered, their action on wood, lignin, and its model compounds having been fairly thoroughly investigated.

Most fungi causing the decay of wood belong to one of the classes of higher fungi (*Basidiomycetes*), but there are also certain wood-decomposing fungi which belong to the class of *Ascomycetes*. Two main types of wood-decomposing fungi, usually referred to as brown rot and white rot, are distinguished. When wood is infected by brown rot, cellulose and other carbohydrate components are preferentially decomposed, while lignin remains relatively unchanged and the decaying wood acquires a brown colour. Infection with white rot results in the decomposition of all the components of wood, and as decay proceeds the residue becomes paler in colour, compared with healthy wood. A list of fungal species belonging to these two groups has been published [1,22] and in addition 126 species of wood-decomposing fungi have been characterised in detail in a review by Nobles [23].

In 1928 Bavendamm [24] observed that white rot fungi cultured on an agar medium containing gallic or tannic acid produce a dark zone around and below the mycelial films, while brown rot fungi do not generate such a zone. This reaction, which has been called the Bavendamm reaction, was subsequently widely used to classify the wood-decomposing fungi. Bavendamm attributed the ability of fungi to degrade lignin to the production of phenol oxidase. This conclusion was confirmed in a study by

Davidson et al.[25], who tested 210 species of wood-decomposing fungi in the Bavendamm reaction and established that 96% of the white rot fungi produced the coloured zones, while 80% of the brown rot fungi did not.

A considerable number of studies[23,26-31] were devoted to the determination of enzymes catalysing the oxidation of the simplest phenolic compounds to quinones, which polymerise to give the coloured complexes in the Bavendamm test. It was noted that the enzymes responsible for this reaction are laccase†[27-29], tyrosinase‡[28,29], and peroxidase§[31], but complete certainty with regard to this problem has not yet been reached.

It is noteworthy that hitherto no systematic studies have been made on the enzymes of wood-decomposing fungi. The available literature data are of a general kind and frequently contradictory. The studies in this field have been examined in detail in monographs by Schubert[7] and Shivrina[32]. It was established that white rot fungi produce two main enzymes: laccase and tyrosinase. Furthermore, Lyr showed that 14 of the 182 species of wood decomposing fungi which have been investigated produce peroxidase[33] and proposed a method for its detection[34]. These enzymes catalyse the abstraction of electrons from phenolic substrates. In the presence of laccase and peroxidase one reducing equivalent is removed from the substrate, while in the presence of tyrosinase two reducing equivalents are eliminated simultaneously.

Since the lignin-decomposing white rot fungi produce in most cases intracellular phenol oxidising enzymes, while the taxonomically related brown rot fungi, which do not produce these enzymes, do not decompose lignin, the relation between the capacity to degrade lignin and the phenol oxidase activity of the wood-decomposing fungi appears to be evident[23,31,35-37]. However, later it was shown that brown rot fungi do produce intracellular phenol oxidising enzymes: tyrosinase and an enzyme of the laccase type[38-43], as well as peroxidase[44]. Furthermore, there is evidence[45-50] that the degradation of lignin is due to enzymes which are not phenol oxidases. For this reason, Kirk and Kelman[51] undertook a study of the ability of 18 different white and brown rot fungi to degrade lignin and produce intracellular phenol oxidase capable of oxidising simple phenolic compounds. Among the fungal species investigated, there were "typical" and "atypical" white and brown rot fungi. The results of the investigation showed that the inability of wood-decomposing fungi to oxidise phenols in an agar medium cannot be used as proof that they cannot utilise lignin.

Thus the role of phenol oxidases in the biodegradation of lignins still remains uncertain. The results of the above studies[31,43,44,51] show that both the lignin decomposing white rot fungi and the brown rot fungi which do not decompose lignin produce phenol oxidising enzymes and that certain brown rot fungi produce more phenol oxidases than white rot fungi. One may therefore conclude that, if the phenol oxidising enzymes from the white rot fungi do not act on lignin in a manner different from that of the phenol oxidising enzymes of the brown rot fungi, the above differences in the ability of both groups of fungi do degrade lignin may depend on the presence of certain other enzymatic systems.

The results of macroscopic studies[52-58] showed that the microbiological degradation of woody tissue begins with the cell lumens in which the fungal hyphae are located and spreads to the region of the middle lamella. In particular, Schmid and Liese[57] established in the course of an electron microscope analysis that woody material is removed essentially layer by layer, which makes the cell walls gradually thinner, while lignin in the middle lamella and in the corners of the cells is apparently relatively resistant to enzymatic attack. On the other hand, Wilcox[58] established that the action of the cellulolytic enzymes of the white rot fungus *Polyporus versicolor* is initially restricted to the surfaces of the cell walls adjoining the lumen, and, as cellulose is removed, gradually spreads to other layers of the cell wall. On the other hand, the cellulolytic enzymes of the brown rot fungi *Poria monticola* and the lignin decomposing enzymes of the white rot fungus can penetrate the cell wall and act within it. The author attributed these differences in the cellulolytic enzymes to their molecular size and chemical properties.

It is noteworthy that, although the principal characteristics of the degradation of wood by various species of brown rot fungi are general, nevertheless the action of each species has its characteristic features due to different enzymatic activities[59]. This is responsible for the differences in the rate of decomposition of wood by various species of brown rot fungi.

III. REACTIONS OF NATURAL AND ISOLATED LIGNINS UNDER THE INFLUENCE OF WOOD DECOMPOSING FUNGI

Studies on the changes in lignin under the influence of wood-decomposing fungi were made either on preparations isolated after incubating various isolated lignins with white rot fungi in synthetic liquid culture media or on preparations extracted by neutral solvents from wood subjected to the action of white rot. In most cases the preparations isolated from liquid culture media and from decayed wood undergo analogous changes in relation to the initial control lignin (cf. Tables 1 and 2) and can therefore be treated together. However, one should bear in mind[13] that (1) the regeneration and purification of the preparations after the incubation of isolated lignins with microorganisms can lead to a series of additional changes and (2) that lignin isolated from decayed wood may differ from the control preparation not only in consequence of the changes due to the action of fungi but also due to the method of extraction, which usually differs from the method used to isolate the control preparation.

A study of the action of various brown rot fungi on sprucewood established that nitrobenzene oxidation of decomposed wood gives a higher yield of vanillin compared with healthy wood[60]. Leopold[61] investigated the products of the nitrobenzene oxidation of wood at different stages with decomposition by brown rot fungi and observed a successive decrease of their yield, although the oxidation products contained the same aldehydes and in virtually the same proportions as the products of the oxidation of healthy wood. The author believes that the decrease of the yield of vanillin is due to the preferential enzymatic attack on the "open" lignin structures, i.e. not condensed in the 5-position of the aromatic ring, which constitute the main source of vanillin in nitrobenzene oxidation. A decrease

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† *p*-Diphenol: oxygenoxidoreductase (*p*-diphenol oxidase), EC 1.10.3.2.

‡ *o*-Diphenol: oxygenoxidoreductase (*o*-diphenol oxidase), EC 1.10.3.1.

§ Donor: hydrogen-peroxideoxidoreductase, EC 1.11.1.7.

of the yield of vanillin in the nitrobenzene oxidation of pinewood decomposed by brown rot fungi was also noted by Enkvist et al.[62]

Higuchi et al.[63] studied lignin preparations isolated from beechwood which had been acted upon by various brown and white rot fungi in the course of five months. The authors established that the overall yield of aldehydes in the nitrobenzene oxidation of decayed wood is lower than in the case of healthy wood, and that the yield with respect to lignin is lower for wood subjected to the action of white rot fungi than for wood subjected to the action of brown rot fungi. Moreover, an increase of the molar proportions of syringaldehyde and vanillin in the products of the nitrobenzene oxidation of decayed wood in relation to healthy wood was observed.

The decrease of the yield of vanillin in the nitrobenzene oxidation of the isolated lignins subjected to the action of white rot fungi was also pointed out by Ishikawa et al.[64] They investigated the changes in the native Brauns lignin and milled-wood lignin (MWL), isolated from pinewood and sprucewood, as a result of their incubation with white rot fungi. In the experiments a study was made of both "phenol oxidase-rich" (*Polyporus hirsutus*, *Polyporus versicolor*, and *Poria subacida* J247) and "phenol oxidase-deficient" (*Poria subacida* N199, *Fomes fomentarius*, *Fomes annosus*, and *Trametes pini*) white rot fungi. It was established that the degradation of lignin by the white rot fungi leads to a decrease of the number of methoxy-groups and an increase of the content of the overall and phenolic hydroxy-groups, carbonyl groups, and carboxy-groups (Table 1).

Table 1. Results of an analytical study of the initial lignins and lignins acted upon by white rot fungi* (according to Ishikawa et al.[64]).

Lignin	Fungal species	Yield, %	Content, %			Content, moles per lignin unit with mol. wt. of 180			Yield of vanillin, %
			C	H	OCH_3	OH_{phen}	CO	COOH	
Pinewood MWL	control	—	63.70	6.29	15.5	0.24	0.20	0.024	20.0
Ditto	*Fomes fomentarius*	77.0	61.55	5.77	14.1	0.30	0.27	0.106	15.1
"	*Polyporus versicolor*	61.8	61.41	6.11	10.1	0.32	0.23	0.130	11.0
Native pinewood lignin	control	—	63.85	6.22	14.5	0.32	0.24	0.022	22.6
Ditto	*Fomes fomentarius*	73.5	64.00	6.23	12.1	0.40	0.28	0.125	13.6
"	*Polyporus versicolor*	55.2	61.98	6.08	9.6	0.33	0.20	0.150	10.4

*Culture conditions: synthetic liquid medium containing 1% of lignin, 26–29°C, 13 days.

The study of the infrared spectra of lignin subjected to the action of white rot fungi revealed an increase in absorption at about 1670 cm^{-1}. The increase was attributed to the accumulation in the lignin of conjugated carbonyl and (or) conjugated carboxy-groups. Other investigators[65–67] noted that fungal attack enhances the absorption in the range 1710–1735 cm^{-1}. This band was also assigned to conjugated carbonyl and (or) carboxy-groups.

Ishikawa and Oki[68] showed that native spruce lignin acted upon by H_2O_2 and purified peroxidase preparations isolated from horseradish, radish, and lumps of *Collybia velutipes* N8 mycelia undergoes changes analogous to those discussed above, except that the content of methoxy-groups remains constant.

Ishikawa and Oki[69] investigated the changes undergone by ethanol-lignin from Japanese cedar under the influence of a purified enzymatic solution obtained from mycelial clusters or mycelium-free culture filtrates from *Collybia velutipes* N8 and *Polyporus versicolor*. It was established that enzymatic hydrolysis of ethanol-lignin leads to an almost quantitative removal of ethoxy-groups with a simultaneous increase of the number of alcoholic OH groups and a slight increase of the content of phenolic hydroxyls. No changes were observed in the infrared and ultraviolet spectra as a result of the enzyme action. At the same time a study was made of the transformations of a number of aromatic ether compounds under the influence of a purified enzymatic solution (the results are discussed in Section V). The results enabled the authors to conclude that during fungal attack alkyl–alkyl and alkyl–aryl ether linkages are hydrolysed enzymatically in ethanol-lignin.

Table 2. Results of an analytical study of sprucewood MWL and lignin preparations extracted from sprucewood acted upon by *P. subacida* (according to Hata[66]).

Preparation	Yield, % of lignin in decayed wood	Content, %			Content, moles per lignin unit with mol. wt. of 180			
		C	H	OCH_3	OH_{tot}	OH_{phen}	CO	COOH
MWL	—	62.81	5.88	15.24	1.18	0.25	0.14	0.017
DL-I*	1.1	60.44	5.67	12.32	1.42	0.30	0.21	0.053
DL-II**	2.7	58.54	5.23	11.75	1.67	0.40	0.28	0.106
DL-III***	—	55.01	4.98	9.69	—	—	0.30	0.113

*Lignin extracted with an acetone–water mixture from wood acted upon by *P. subacida* for 3 months.
**Lignin extracted with an acetone–water mixture from wood acted upon by *P. subacida* for 6 months.
***Lignin extracted with water from wood acted upon by *P. subacida* for 6 months.

On the basis of ultraviolet and infrared spectroscopic studies native spruce lignin and lignin extracted by acetone from sprucewood powder acted upon by *Poria subacida*, Fukuzumi[70] concluded that there is an appreciable increase in the number of carbonyl groups in lignin subjected to enzymatic action. Hata[66] investigated preparations of lignin extracted from sprucewood acted upon by *Poria subacida* BII. Compared with spruce MWL, the preparations isolated contained fewer methoxy-groups and more phenolic hydroxyls, carbonyl groups, and carboxy-groups (Table 2). In addition, it was established that, as a result of enzyme action, the number of coniferaldehyde and guaiacylcarbinol groups in lignin diminishes. In the nitrobenzene oxidation of degraded lignins a smaller amount of vanillin and a greater amount of vanillic acid (compared with spruce MWL) is produced, and with increase of the duration of enzyme action, this tendency becomes more pronounced (Table 3). However, the overall yield of these products from degraded lignin is lower than from MWL. In hydrolysis by a dioxan–water

mixture (180°C, 50 min and 140°C, 60 min) degraded lignin gives a higher yield of vanillic acid and a lower yield of coniferyl alcohol, coniferaldehyde, and vanillin compared with MWL. Furthermore, a very small amount of ferulic acid, not detected in the products of the hydrolysis of MWL is produced. The study of free radicals in MWL and in degraded lignins showed that their numbers are approximately the same, but the radicals belong to different types.

Konishi and Inoue [71-74] showed that the enzymes produced in culture filtrates by the fungus *Coriolus versicolor* convert MWL isolated from Sugi sapwood into a water-soluble state without a significant change in its molecular weight, but do not break down lignin into low-molecular-weight compounds. Compared with the initial MWL, the water-soluble lignin contains more COOH groups and fewer alcoholic OH groups. The above changes were attributed to enzymatic attack on the side chains of the phenylpropane units of lignin, which evidently proceeds via a radical reaction.

Table 3. Yields of nitrobenzene oxidation products (% of lignin) (according to Hata [66]).

Preparation	Vanillic acid	Vanillin
Sprucewood MWL	2.2	24.1
DL-I*	4.8	14.9
DL-II**	6.7	10.2

*The designations of the preparations are the same as in Table 2.

Steelink [75,76] established that the action of brown or white rot fungi on wood increases by a factor of 2–3 its content of free radicals and that the wood of deciduous trees attacked by fungi has a higher concentration of free radicals than the wood of conifers. These data were confirmed in a study by Kreitsberg et al. [77]

Ferm et al. [78] investigated the transformations of MWL from Liquidambar (sweetgum) under the influence of partly purified preparations of horseradish and peroxidase and laccase from *Polyporus versicolor* and also of an unpurified enzyme from the brown rot fungus *Poria cocos*. Experiments on the enzymatic oxidation of lignin were carried out in a methylcellosolve–water mixture which dissolves MWL and has only an insignificant influence on the stability of the enzyme preparations employed. ESR showed that each enzyme preparation causes the formation of free radicals of the phenoxy-type. The formation of radicals of a similar type was observed previously [79] on incubation of syringyl compounds with phenol oxidising enzymes (see Section V). Furthermore, Ferm et al. [78] reported the preliminary results of a study of the changes in the molecular weight distribution of lignin and lignosulphonate under the influence of phenol oxidising enzymes. It was shown by gel permeation chromatography that phenol oxidising enzymes cause an increase in molecular weight. On this basis, the authors suggested that phenol oxidising enzymes can be involved in later stages of the microbiological degradation process and not in the initial depolymerisation reactions.

Ishihara and Miyazaki [80] investigated the changes in the molecular weight of maple MWL as a result of incubation with laccase B obtained from the filtrate of a *Polyporus versicolor* culture and concluded on the basis of the results that this enzyme can polymerise and depolymerise lignin, the first function being dominant.

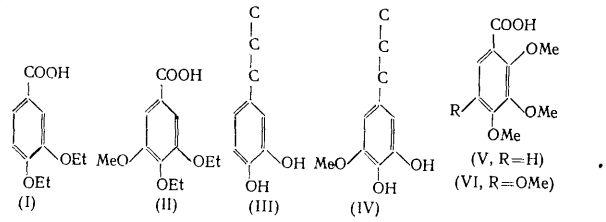
Kirk and Lundquist [67] made a comparative study of MWL preparations isolated from healthy cambium and cambium acted upon by *Polyporus versicolor* (32% weight loss) of sweetgum wood. They established that these preparations do not show distinct differences as regards elemental composition and the content of OCH_3 groups, ultraviolet and infrared spectra, $\Delta\epsilon$ curves, molecular weight distribution curves, and the composition of the ethoxybenzoic acids formed on degradation of lignin by the ethylation–oxidation method [81]. The results showed that the lignin isolated from decayed wood by mechanical milling (27% yield) does not undergo significant changes. This, however, does not allow a conclusion concerning the degree of change of the entire lignin remaining in the decomposed wood. Nevertheless the authors suggested that in the decay of wood by the fungus *Polyporus versicolor* only a limited proportion of the lignin is subjected to enzyme action and is removed before the decay spreads to other parts of the lignin.

Kirk and Lunquist also investigated the substances extracted from healthy and decayed wood with a 2:1 benzene–ethanol mixture and then with 96% ethanol (their yields were 3.3 and 3.6% of the wood respectively). The high-molecular (molecular weight >400) fractions (the so called "extractive lignin") obtained as a result of gel filtration on Sephadex G-25 were investigated by ultraviolet and infrared spectroscopy. The experimental results showed that these preparations consist of lignin and revealed differences between the extractive lignin from healthy and decayed wood. An appreciable absorption at 1730 cm^{-1} was noted in the infrared spectrum of lignin extracted from decayed wood. It was established that this band is due to the chemical changes caused by the fungi and not by the presence of non-lignin impurities. The band could not be assigned accurately, although the authors suggest that absorption in this region may be attributed to non-conjugated carbonyl groups and non-conjugated carboxy-groups. It is interesting to note that the changes in lignin leading to the appearance of the 1730 cm^{-1} band in its infrared spectrum are not accompanied by appreciable changes in the ultraviolet spectrum. This is clearly evidence that enzyme action does not result in the formation of appreciable amounts of chromophoric systems whose spectroscopic properties differ greatly from those of the chromophores present initially in the lignin (aryl-conjugated carboxy-groups, aryl-conjugated carbonyl groups, *p*-benzoquinonoid residues, and others).

Interesting results were obtained in recent years in studies by oxidative degradation methods on the lignin remaining after wood has been acted upon by brown rot fungi (the so called enzymatically liberated lignin).

According to the results of a number of investigators [60,62,82-87], the action of brown rot fungi on lignin greatly reduces its content of methoxy-groups. Kirk and Adler [81,88] undertook a study of the structural changes leading to a decrease of the content OCH_3 groups. They investigated the lignin liberated enzymatically from sweetgum wood acted upon by the brown rot fungus *Lenzites trabea*. After preliminary ethylation, the lignin preparations were subjected to oxidative degradation. The resulting ethoxybenzoic acids were identified by gas chromatography and mass spectrometry. The acids (I)

and (II) were detected in the degradation products of the enzymatically liberated lignin, which indicates the presence in the latter of the *o*-diphenol structures (III) and (IV).



These structures are formed as a result of the fungal demethylation of the lignin units of the guaiacyl and syringyl type respectively. Furthermore, Kirk and Adler boiled a preparation of the enzymatically liberated lignin with 0.2 M HCl solution in a dioxan–water mixture. This treatment led to the cleavage of the alkyl aryl ether linkages with formation of phenolic OH groups. Subsequent ethylation and oxidative degradation gave higher yields of acids (I) and (II). Thus fungal attack does not lead to the demethylation of units with a free phenolic hydroxyl alone. However, non-phenolic residues are demethylated to a smaller extent than the corresponding phenolic residues. It was also established that both phenolic and non-phenolic structures of the syringyl type are demethylated more vigorously than the corresponding structures of the guaiacyl type. The preferential demethylation of units of the syringyl type can evidently be explained by the fact that they contain two methoxy-groups, so that the demethylating enzymatic system is better able to come into contact with them.

Thus *Lenzites trabea* demethylates both free and etherified units of the guaiacyl and syringyl type in lignin. According to the authors [81,88], the demethylation can occur as a result of the direct oxidation of the methyl group, which is then eliminated as formaldehyde, leaving behind a free phenolic OH group.

Kirk et al. [89] made a comparative study of methoxylated aromatic carboxylic acids formed in the degradation of enzymatically liberated lignin and MWL from sweetgum by the method of Larsson and Miksche [90-92]. The acids (V) and (VI), formed from structures hydroxylated as a result of fungal action, were identified among the degradation products of the enzymatically liberated lignin. Hydroxylation takes place in the *ortho*-position relative to the side chains of the phenylpropane units of lignin. However, neither the mechanism of this process nor the lignin units which undergo hydroxylation (initial guaiacyl and syringyl units or the newly formed *o*-diphenol units) are so far known.

IV. LOW-MOLECULAR-WEIGHT PRODUCTS OF THE MICROBIOLOGICAL DEGRADATION OF LIGNIN

Henderson [93] showed that incubation for six months of sprucewood and birchwood fillings, subjected to preliminary extraction, with the white rot fungi *Polystictus versicolor* and *Trametes pini* led to the liberation of vanillic acid in the first case and a mixture of vanillic and syringic acids in the second. Higuchi et al. [63] reported the presence of coniferaldehyde, vanillin, and syringaldehyde in the alcohol–benzene extract of beechwood powder infected by white rot fungi. Fukuzumi [70] investigated the products of the enzymatic degradation of native sprucewood lignin by the fungus *Poria subacida* using paper chromatography and reported the presence of 4-hydroxy-3-methoxypyruvic acid. Furthermore, β-coniferyl guaiacylglyceryl ether and a compound resembling vanillic acid were detected in the acetone and methylene chloride extracts of sprucewood powder decomposed by the same fungus.

An extensive study on the low-molecular-weight products of the enzymatic degradation of lignin was carried out by Ishikawa et al. [64] They incubated native lignin and MWL preparations isolated from pinewood and sprucewood with various white rot fungi in liquid culture media. The acid fractions of the ether extracts of the lignin degradation products were studied by paper chromatography. The products identified are listed in Table 4.

Table 4. Low-molecular-weight products formed when pinewood and sprucewood lignin is acted upon by white rot fungi* (according to Ishikawa et al. [64]).

	Vanillic acid	*p*-Hydroxybenzoic acid	Ferulic acid	4-Hydroxy-3-methoxyphenylpyruvic acid enolic tautomer)	*p*-Hydroxycinnamic acid	Guaiacylglycerol	Vanillin	Dehydrodivanillin	Coniferaldehyde	*p*-Hydroxycinnamaldehyde	β-Coniferyl guaiacylglyceryl ether
R_f	0.08	0.11–0.12	0.17–0.18	0.18–0.19	0.22–0.24	0.42–0.44	0.45–0.47	0.53–0.55	0.60–0.61	0.66–0.68	0.80–0.82
A** NL	+	+			+		+	+	+	+ (?)	
A** MWL	+	+			+		+	+ (?)	+		
B*** NL	+	+	+	+	+	+	+	+	+	+	+
B*** MWL	+	+	+	+	+	+	+	+	+	+	+
Control****		+			+						

*Conditions: culture medium containing 1% of lignin, 27°C, 28 days. Solvent for paper chromatography—butanol saturated with 3% ammonia.

**A—species rich in phenol oxidase (*Polyporus hirsutus*, *Polyporus versicolor*, and *Poria subacida* J247).

***B—species deficient in phenol oxidase (*Poria subacida* N199, *Fomes fomentarius*, *Fomes annosus*, and *Trametes pini*).

****Medium without lignin after degradation by fungi of group A or B.

The results of this investigation showed that ferulic acid, 4-hydroxy-3-methoxyphenylpyruvic acid, guaiacylglycerol, and its coniferyl ether are probably more readily metabolised by phenol oxidase-rich microorganisms (group A), compared with other intermediates. The presence of β-coniferyl guaiacylglyceryl ether in the enzymatic degradation products of lignin and also the formation of coniferaldehyde, α-hydroxypropiovanillone, and vanilloyl methyl ketone in the acidolysis of the phenolic fraction of the lignin degradation products constitutes proof, according to the authors, that lignin contains β-coniferyl guaiacylglyceryl ether linkages.

As noted above, Kirk and Lundquist [67] extracted the cambial components of sweetgum wood, both healthy and acted upon by *Polyporus versicolor*, with a 2:1 benzene–ethanol mixture and then with 96% ethanol. The extracted products were subjected to gel filtration on Sephadex G-25

and the resulting low-molecular-weight (monomeric) fraction was separated by paper chromatography. Vanillin, syringaldehyde, vanillic and syringic acids, coniferylaldehyde and sinapaldehyde were identified in the monomeric fraction of the substances extracted from the decayed wood. Since the same substances were found in approximately the same amounts also in products extracted from the healthy wood, the authors suggest that their formation cannot be attributed to fungal attack. Evidently the low-molecular-weight compounds are formed as a result of hydrolysis during decay and not as a result of the decomposition of the phenylpropane units of lignin.

Kirk and Lundquist attempted to detect in the monomeric fraction of the substances extracted from decayed wood guaiacylglycerol, syringylglycerol, and 4-hydroxy-3-methoxyphenylpyruvic acid, i.e. the compounds which Ishikawa et al.[64] identified among the products of the enzymatic degradation of lignin. These compounds were not detected, which, according to Kirk and Lundquist, requires the amendation of the results of earlier studies. However, since *Polyporus versicolor* is a phenol oxidase-rich species of the white rot fungi, the results of Kirk and Lundquist are not inconsistent with those of Ishikawa et al. (Table 4).

Ishihara and Miyazaki[80] incubated maple MWL with a preparation of laccase B obtained from the filtrate of a *Polyporus versicolor* culture for 4 days at 30°C. 2,6-Dimethoxy-*p*-benzoquinone, the formation of which has been observed previously in the enzymatic degradation of a number of model compounds[94] (see Section V), was identified among the low-molecular-weight degradation products of lignin.

Antropova and coworkers[95] investigated 548 strains of wood decomposing fungi belonging to different taxonomeric groups¶. In these experiments the sulphate lignin from aspenwood served as the only source of carbon. The results of the chromatographic study of the monomeric lignin degradation product revealed some specificity in the action of the fungi investigated. Thus aldehydes and certain acids predominated in the cultures of *Mucor* species, while the main products of the metabolism of fungi of the *Trichoderma* species were ketones and benzoic and vanillic acids. *Aspergillus* species produced coniferaldehyde, *p*-hydroxybenzaldehyde, dehydrodivanillin, ketones, and acids, including certain acids which had not been detected in the presence of *Mucor* and *Trichoderma* species. Alcohols, absent in the presence of fungi of the *Mucor*, *Trichoderma*, and *Aspergillus* species, as well as phenols, certain aldehydes, ketones, and acids were detected in the products of the metabolism of fungi of the *Penicillium* and *Fusarium* species.

The study of the lignin-decomposing properties of micromycetes led to the discovery of two most active strains, *Mucor* sp. 15157 and *Penicillium* sp. 50311, exhibiting laccase and phenolase activities respectively[96].

In the degradation of lignin by *Mucor* sp. 15157 the following products were detected in the culture liquid: *p*-hydroxybenzoic, benzoic, *p*-hydrozycinnamic, vanillic, syringic, sinapic, protocatechuic, homoprotocatechuic, cinnamic, 4-hydroxy-3-methoxyphenylpyruvic, and ferulic acids, vanillin, protocatechuic aldehyde, and a number of unidentified substances. In the determination of the quantitative yield of the main lignin decomposition products *p*-hydroxybenzoic acid was detected in an amount of 0.4% on the 7–12th day of the growth of the fungus, while on the 18th day the yield reached 2.0%. Vannillic acid appeared on the 7th day in an amount of 0.06%, its amount gradually increasing and reaching 0.13% on the 20th day, while on the 23rd day it rose sharply to 3.5% after which it fell and varied in the range 0.06–0.1%. Syringic acid appeared only on the 28th day, in an amount of 0.04–0.1%. The yield of the remaining substances varied in the range 0.04–0.1%.

In the degradation of lignin by *Penicillium* sp. 50311 the following substances were detected in the culture liquid, *p*-hydroxybenzoic, benzoic, vanillic, 4-hydroxy-3-methoxyphenylpyruvic, ferulic acid, sinapaldehyde, vanillyl alcohol, 3-hydroxyphenyl-1-propanol, guaiacyl-3-propanol, guaiacyl-2-propanol, pyrogallol, and phenol. The amount of vanillic acid in the culture liquid gradually increased: its content on the 10th day was 0.09%, reaching a maximum level of 0.89% on the 18th day, after which it gradually fell; the same happened with *p*-hydroxybenzoic acid: its content was 0.06% on the 3rd day, 0.5% on the 30th day, after which it fell. The amount of syringic acid reached a maximum of 3.5% on the 30th day, after which it decreased to 0.06%.

V. MICROBIOLOGICAL DEGRADATION OF PHENOLIC COMPOUNDS STRUCTURALLY RELATED TO LIGNIN. POSSIBLE PATHWAYS IN THE MICROBIOLOGICAL DEGRADATION OF LIGNIN

The studies on the enzymatic transformations of phenolic compounds structurally related to lignin discussed below yielded information, which led to hypotheses concerning the mechanism of the transformations of lignins in the course of fungal attack.

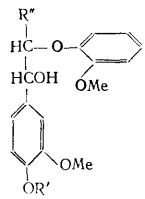
As early as 1956, Minami and Fukuzumi[97] pointed out the reducing function of *Polystictus sanguines*, having detected benzaldehyde in the metabolic products of benzoic acid. Later Fukuzumi et al.[98] reported the reduction of veratric acid to veratraldehyde as a result of incubation with *P. sanguines*.

Henderson and coworkers[99] investigated the transformations of certain aromatic acids under the influence of *Polystictus versicolor* and showed that these fungi produce an intracellular alcohol dehydrogenase. *Polyporus versicolor* reduced *m*- and *p*-methoxybenzoic, veratric, and β-naphthoic acids to the corresponding aldehydes and alcohols. Only alcohols were detected among the products of the enzymatic transformations of *o*-methoxybenzoic and benzoic acids. The corresponding alcohols were also obtained from *o*- and *p*-hydroxybenzaldehydes. 2,4-Dimethoxybenzoic, phenylacetic, and α-naphthoic acids were not reduced. The rate of reaction varied as a function of the position and nature of the substituent in the aromatic ring. Furthermore, it was shown that 2,4-dimethoxybenzoic, and *o*-, *m*-, and *p*-methoxybenzoic acids were demethylated to a slight extent to the corresponding hydroxy-compounds, while cinnamic, benzoic, and phenylacetic acids were hydroxylated in the *p*-position, the last two acids only to a limited extent. Some degradation of the aromatic structure was observed in the course of the metabolic transformations of cinnamic, β-naphthoic, and *p*- and *o*-hydroxybenzoic acids.

¶ Some of the *Mucor*, *Aspergillus*, and *Penicillium* species comprise soil fungi and are incapable of decomposing wood by themselves.

Shimazono and Nord[100] established that *P. versicolor* under aerobic conditions reduces *p*-methoxybenzoic acid to the corresponding aldehyde and alcohol. Raman and Shanmugasundaram[101] reported that cultures of the fungus *Aspergillus niger* convert in the presence of glucose up to 50% of benzoic acid, 35% of *o*-aminobenzoic acid, and 10% of *p*-aminobenzoic acid into the corresponding aldehydes. *o*- and *p*-Hydroxybenzoic acids were not reduced to the aldehydes. Furthermore, under anaerobic conditions benzaldehyde was reduced to benzyl alcohol, but other aldehydes did not undergo a similar reaction.

Henderson and coworkers[102] established that *Polystictus versicolor* produces an intracellular alcohol oxidase, which can oxidise primary aromatic alcohols (benzyl alcohol and its *p*-methoxy, *m*-methoxy, 3,4-dimethoxy-, 4-hydroxy-3-methoxy, *o*-hydroxy-, and *p*-hydroxy-derivatives, 4-hydroxy-3-methoxycinnamyl alcohol, and β-naphthylmethanol) to the corresponding aldehydes, but does not oxidise secondary alcohols [1-(3,4-dimethoxyphenyl)ethanol, 1-(4-hydroxy-3-methoxyphenyl)ethanol, and 1-(4-methoxyphenyl)ethanol].



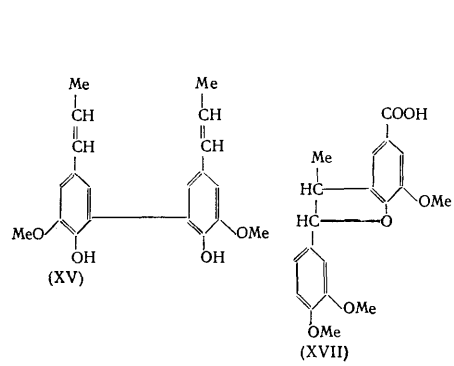
(VII; R′=R″=H)
(VIII; R′=H; R″=CH_2OH)
(IX, R′=CH_3; R″=H)
(X, R′=CH_3; R″=CH_2OH)

In the course of a study of the fungal metabolic transformations of model compounds for lignin, Henderson and coworkers[103] established that the mycelial cells of *P. versicolor* metabolised the β-guaiacyl ether of guaiacylglycol (VII), and β-guaiacyl guaiacylglyceryl ether (VIII) but did not metabolise the β-guaiacyl ether of veratrylglycol (IX) and β-guaiacyl vertrylglyceryl ether (X). The authors noted that the fungus can methylate the phenolic OH groups. Thus the metabolic transformations of compound (VII) yielded veratryl alcohol. Veratraldehyde and veratryl alcohol were also formed as a result of the metabolic transformations of *p*-hydroxybenzoic acid, protocatechuic acid, vanillin, and vanillyl alcohol. None of the compounds (VII)–(X) was oxidised by the intracellular alcohol oxidase of *P. versicolor*.

Ishihara and Miyazaki[104] subjected vanillic acid to the action of the unpurified enzyme from *P. versicolor* and isolated from the reaction mixture a yellow crystalline product melting at 225–226°C. The study of the ultraviolet, infrared, NMR, and mass spectra and analysis of the oxidative degradation products established that this compound is 6-(4′-carboxy-2′-methoxyphenoxy)-2-methoxy-1,4-benzoquinone[105].

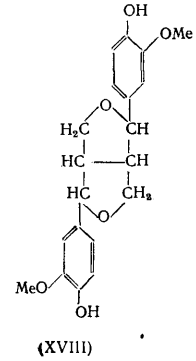
On the basis of the results of the study of the enzymatic degradation of lignin, Fukuzumi[70,106] suggested that lignin decomposes via β-ethers of guaiacylglycerol, β-hydroxyconiferyl alcohol, and 4-hydroxy-3-methoxyphenylpyruvic acid under the action of enzymes from *Poria subaciua*. Fukuzumi suggested that compounds resembling vanillic acid are formed as a result of the cleavage of the side chain of guaiacylpropanones under the influence of the fungal oxidase. He confirmed the presence of homogentisic acid in the culture medium of *P. subacida*.

Ishikawa et al.[107] investigated the transformations of a number of aromatic compounds related to lignin under the influence of *Polyporus versicolor* and *Fomes fomentarius*, which belong to the class of phenol oxidase-rich and phenol oxidase-deficient species of white rot fungi. Vanillyl alcohol (XI), guaiacylmethylmethanol, 4-hydroxy-3-methoxyphenylpyruvic acid (XII), coniferaldehyde (XIII), coniferyl alcohol (XIV), dehydrodi-isoeugenol (XV), guaiacylglycerol (XVI), and its β-guaiacyl ether (VIII) together with certain veratryl and *p*-hydroxyphenyl analogues of these compounds, as well as Erdtman's acid (XVII), pinoresinol (XVIIIa), and symplocosigenol (XVIIIb) were used as substrates.



(XV)

(XVII)



(XVIII)

The studies established that in general guaiacyl compounds were metabolised faster while *p*-hydroxyphenyl compounds were somewhat more resistant to fungal attack under the same conditions. *p*-Hydroxycinnamic, *p*-hydroxyphenylpyruvic, ferulic, and 4-hydroxy-3-methoxyphenylpyruvic acids, coniferyl aldehyde, coniferyl alcohol, isoeugenol, and guaiacylglycerol were particularly rapidly metabolised. After the incubation of these compounds with *P. versicolor* for 4–5 days, only small amounts of the substrate were detected in the filtrates. However, the amount of the metabolic products accumulated in the reaction medium was also comparatively small. It is likewise noteworthy that a proportion of the compounds investigated were converted into polymers. *p*-Hydroxycinnamic, *p*-hydroxyphenylpyruvic, ferulic, and 4-hydroxy-3-methoxyphenylpyruvic acids, Erdtman's acid, coniferaldehyde, coniferyl alcohol, isoeugenol, dehydrodi-isoeugenol, simplocosigenol, and pinoresinol were more readily polymerised by the fungus *P. versicolor* than by *F. fomentarius*. The principal metabolic products formed from the substrates tested are listed in Table 5.

The main products of the enzymatic degradation of the compounds employed are vanillin and vanillic acid, their yield being higher for the degradation monomers and not dimers. Since the authors did not report their control experiments involving the incubation of the medium and substrate alone, this suggested[13] that vanillin and vanillic acids might have been formed as a result of the autoxidation of the specimens or contamination of the substrates.

Both *P. versicolor* and *F. fomentarius* converted β-guaiacyl guaiacylglyceryl ether (VIII) into guaiacylglycerol (VI) and guaiacol. The guaiacylglycerol formed in this way was converted further by both fungi into vanillic acid via 4-hydroxy-3-methoxyphenylpyruvic acid (XII) and vanillin, but the acid (XII) was not detected in the culture medium of *P. versicolor*.

p-Hydroxyphenyl derivatives undergo similar transformations (*p*-hydroxybenzaldehyde and *p*-hydroxybenzoic acid are formed from *p*-hydroxycinnamic and *p*-hydroxyphenylpyruvic acids, while *p*-hydroxybenzaldehyde is oxidised to *p*-hydroxybenzoic acid).

It was noted at the same time that guaiacyl compounds are reduced under the influence of enzymes. In particular, in the presence of *F. fomentarius* vanillyl alcohol (XI) was detected in the products of the metabolic transformations of vanillin, vanillic acid, acetovanillone, and isoeugenol. Furthermore, *p*-hydroxybenzoic, *p*-hydroxycinnamic, and ferulic acids as well as *p*-hydroxybenzaldehyde were converted enzymatically into the corresponding aldehyde or alcohol.

Table 5. Products of the enzymatic degradation of a number of phenolic compounds structurally related to lignin (according to Ishikawa et al.[107]).

Substrate	Vanillin (XIX)	Dehydrodivanillin (XX)	Vanillic acid (XXI)	Ferulic acid (XXII)	Coniferaldehyde (XXIII)	4-Hydroxy-3-methoxyphenylpyruvic acid (XII)
Vanillin		+	+			
Vanillyl alcohol	+	+	+			
Acetovanillone	+	+	+			
Guaiacylmethylmethanol	+	+	+			
Ferulic acid	+	+	+			
4-Hydroxy-3-methoxyphenylpyruvic acid	+	+	+			
Erdtman's acid*	+	+	+			
Pinoresinol*	+	+	+			
Symplocosigenol*	+	+	+			
Dehydrodiisoeugenol*	+	+	+			
Coniferaldehyde	+	+	+	+	+	
Coniferyl alcohol	+	+	+	+	+	
Isoeugenol	+	+	+			
Guaiacylglycerol	+		+			+

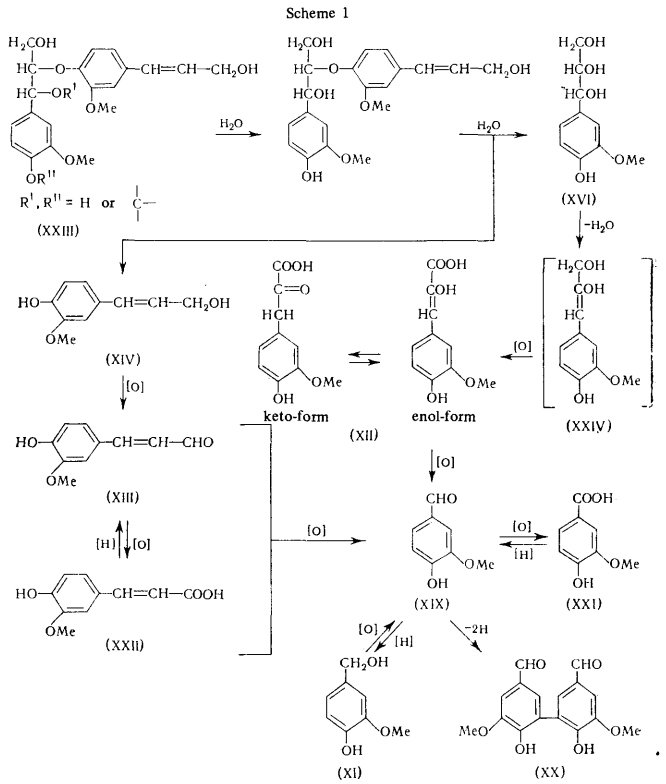
*Compound relatively resistant to fungal attack.

It was also noted that the action of both fungi leads to partial demethoxylation of a number of methyl derivatives of the *p*-hydroxyphenyl and guaiacyl compounds investigated with subsequent oxidation of the demethylated products. (Subsequent studies[108-111] demonstrated the demethylation of various methoxylated aromatic compounds, occurring as a result of fungal attack.)

The results obtained in studies on the enzymatic degradation of lignin and structurally related phenolic compounds enabled Ishikawa, Schubert, and Nord to suggest that the initial stage in fungal attack leads to the loss of methoxy-groups and the cleavage of certain types of ether bonds as well as the degradation of vanillin forming lignin structures. The low-molecular-weight products formed as a result are degraded further to vanillic acid, which can then be metabolised via the formation of protocatechuic acid.

The β-aryl guaiacylglyceryl ether units (XXIII) of lignin are degraded via guaiacylglycerol (XVI), β-hydroxyconiferyl alcohol (XXIV), and 4-hydroxy-3-methoxyphenylpyruvic acid (XII). The enolic form of this acid, which is most sensitive to the action of oxidases, is converted further into vanillin and vanillic and oxalic acids as a result of the oxidative cleavage of its propane side chain. Coniferyl aldehyde and ferulic acid, which are also formed on decomposition by fungi of the lignins in the wood of conifers, are converted similarly into vanillin and vanillic acid (Scheme 1). However, the hypothesis that compounds

Scheme 1



with the phenylpropane structure are intermediates in the degradation of lignin by white rot fungi and that an appreciable proportion of the polymeric lignin breaks down in the way shown in Scheme 1 is based essentially only on the detection of small amounts of monomeric phenylpropane compounds formed when isolated lignin is incubated with white rot fungi (see Section IV). Nevertheless, small amounts of these products might have been formed from the "side groups" or from secondary structural elements and not from the block of the phenylpropane units of the polymer itself. Furthermore, despite the quantitative importance of the β-aryl glyceryl ether linkages in lignin, the available data show, that their cleavage can liberate only a small amount of monomeric aromatic compounds even when appreciable depolymerisation takes place. (For example acidolysis of lignin, which leads to the quantitative cleavage of β-alkyl aryl ether linkages, the yield of monomeric degradation products is about 11% of the lignin[112].) Thus one may conclude that the cleavage of the β-aryl arylglyceryl linkages by the white rot fungi evidently cannot result in the liberation of appreciable amounts of monomeric products.

Ishikawa et al.[113] also investigated the enzymatic degradation of guaiacylglycerol (XVI), β-hydroxyconiferyl alcohol (XXIV), and 4-hydroxy-3-methoxyphenylpyruvic acid (XII) by purified enzyme preparations obtained from the mycelial clusters and the filtrates of *Fomes fomentarius* and *Collybia velutipes* cultures freed from mycelia. These preparations included mainly tyrosinase, an enzyme of the laccase type, and peroxidase. The authors observed enzymatic transformations of compounds

(XVI), (XXIV), and (XII) to vanillic acid via vanillin. Furthermore, the formation of (XII) from (XVI) and (XXIV) and the formation of compounds of type (XXIV) from (XVI) was demonstrated. The results were regarded by the authors as further evidence indicating that guaiacylglycerol, formed in the enzymatic degradation of the β-aryl guaiacylglyceryl ether linkages of conifer lignin, is converted further into vanillic and oxalic acids via β-hydroxyconiferyl alcohol, 4-hydroxy-3-methoxyphenylpyruvic acid, and vanillin as a result of the oxidative cleavage of the propane side chain.

Ishikawa and Oki [68] investigated the degradation of a number of aromatic compounds by purified preparations of peroxidase obtained from horseradish, radish, and clusters of *Collybia velutipes* N8 mycelia. The enzymatic transformations of the compounds under the influence of peroxidase involved both dehydropolymerisation and oxidative cleavage of the side chains. An example of the first process is provided by the formation of polymers from vanillin, acetovanillone, guaiacylmethylmethanol, eugenol, isoeugenol, ferulic acid, coniferyl aldehyde, guaiacylglycerol, coniferyl alcohol, Erdtman's acid, dehydrodi-isoeugenol, pinoresinol, symplocosigenol, and β-guaiacyl guaiacylglyceryl ether, while the formation of vanillin and dehydrodivanillin from vanillyl alcohol, ethyl vanillyl ether, β-hydroxyconiferyl alcohol, and 4-hydroxy-3-methoxyphenylpyruvic acid is an example of the second process. (It is noteworthy that the methyl derivatives of all these compounds were regenerated quantitatively from the peroxidase solutions after incubation for 2 h.) The authors showed that the degradation is accelerated by the addition of H_2O_2 and an increase of the enzyme concentration, being inhibited by heating (the optimal pH is 5.3 to 5.5).

Ishikawa and Oki [69] subjected a number of aromatic ether compounds (β-guaiacyl guaiacylglyceryl ether, ethyl vanillyl ether, and methyl veratrylmethyl ether) to the action of purified enzyme solutions obtained from mycelial clusters or filtrates of the *Collybia velutipes* N8 and *Polyporus versicolor* cultures freed from mycelia. It was established that the ether linkages in these compounds are hydrolysed with the formation of the corresponding alcohols. In particular, after incubation of compound (VIII) with a 30-day filtrate of the *C. velutipes* culture (25°C, second day), 20–30% of the substrate was converted into guaiacylglycerol. The study of the action of inhibitors and the pH on the enzymatic hydrolysis of ethyl vanillyl ether to vanillyl alcohol led the authors to the conclusion that the enzyme responsible for the hydrolysis of aromatic ether compounds is not of the metal-containing type such as laccases and peroxidases. Fukuzumi and Shibamoto [49] studied the degradation of β-guaiacyl veratrylglyceryl ether by the partly purified enzyme from *Poria subacida*. The reaction was carried out at pH 4.0 in an acetate buffer solution at 30°C in the course of two days. Chromatographic studies of the reaction mixture revealed the presence in the latter of guaiacol and an unidentified compound, which the authors believed to be veratrylglycerol or 3-hydroxy-1-(3,4-dimethoxyphenyl)-2-propanone.

In the course of subsequent experiments Fukuzumi et al. [50] showed that the amount of guaiacol liberated when compound (X) is acted upon by the partly purified enzyme from the mycelium of *F. subacida* increases significantly when the reaction is performed in the presence of the reducing coenzyme NADH (reduced nicotinamide-adenine dinucleotide). The authors also reported the formation of guaiacylglycerol (XVI) on incubation of compound (X) with the enzyme of *P. subacida* in the presence of NADH. The latter finding shows that, apart from the enzymatic cleavage of the β-alkyl aryl ether linkage, *para*-demethylation takes place. However, the identification of compound (XVI) was based exclusively on thin-layer chromatographic data with one solvent system and therefore cannot be regarded as adequate. Fukuzumi et al. [50] reported that the enzyme system employed in these experiments does not attack the β-alkyl aryl ether linkage in compounds containing the α-keto-group, while the β-ether linkage in ethylene glycol and glycerol structures is cleaved. Evidently the presence of the hydroxybenzyl-group in the side chain is a factor which determines the possibility of the cleavage of the β-ether linkage by the enzyme system from *P. subacida*.

The authors suggested that the cleavage of the β-alkyl aryl ether linkage can proceed via two possible mechanisms, one of which invoves the direct hydroxylation of the β-carbon atom in the presence of NADH and oxygen. This reaction should lead to the formation of guaiacol and veratryl- or guaiacyl-dihydroxyacetone (the latter was not identified by the authors, who suggest that it may be reduced to guaiacylglycerol). The second involves a hydrolytic reaction of β-guaiacyl guaiacylglyceryl ether, which is formed via the demethylation of the initial substrate and is more readily hydrolysable than β-guaiacyl veratrylglyceryl ether. The low yield of guaiacol in the enzymatic cleavage of compound (X) in the presence of NADH (at most 30%) is caused, according to Fukuzumi et al., by an enzyme stereospecific in relation to the *erythro*- and *threo*-forms of β-guaiacyl veratrylglyceryl ether.

Thus the results of the above studies indicate the possibility of the existence of an enzyme system which cleaves β-aryl arylglyceryl linkages in lignin. However, the methodological defects of these experiments make it impossible to characterise sufficiently rigorously this enzyme system and the mechanism of its action on lignin.

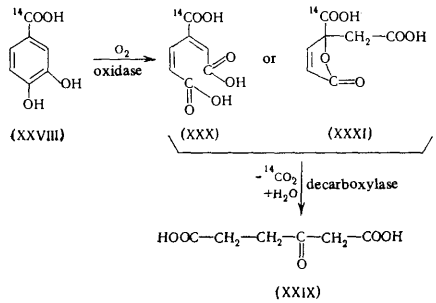
The studies described indicate the ability of the white rot fungi to convert β-aryl guaiacylglyceryl ethers or possibly other structural elements of lignin into monomeric benzenoid compounds of the type of vanillin and vanillic acid. Further transformation of these compounds by the white rot fungi may evidently involve different pathways, an important stage of which is cleavage of the aromatic ring. Data have been published showing that fungal attack involves the cleavage of aromatic rings. Thus Fukuzumi et al. reported that incubation of benzoic acid with the mycelial clusters of *Polystictus sanguineus* results in the formation of acetoacetic acid (XXV) [97] and α-oxogluaric acid [114], which were absent from the control experiment. Subsequently Fukuzumi [115] observed that *Poria subacida* completely metabolised gentisic acid (XXVI) to carbon dioxide. Crowden [116] established that *Polyporos tumulosus* metabolised fully *p*-hydroxyphenylpyruvic, *p*-hydroxyphenylacetic, *p*-hydroxymandelic, *p*-hydroxybenzoic, and protocatechuic acids, and to an extent greater than 50% homogentisic (XXVII), 2,5-dihydroxymandelic, and gentisic (XXVI) acids.

Moore and Towers [117,118] investigated the degradation of phenylalanine and tyrosine by the wood decomposing fungi *Schizophyllum commune*, *Sporobolomyces roseus*, and *Ustilago hordei*. Incubation of the mycelial cells of *S. commune* or of washed cell suspensions of *S. roseus* with ring-labelled phenylalanine led to the formation of $^{14}CO_2$. All three organisms converted labelled phenylalanine into cinnamic, benzoic, *p*-hydroxybenzoic, and protocatechuic acids; furthermore, phenyl-lactic and phenylacetic acids were detected in the metabolic products

of *S. commune*. Among the three fungi investigated, only *S. roseus* exhibited tyrosinase activity, converting tyrosine and *p*-coumaric acid into *p*-hydroxybenzoic and protocatachuic acids. On the basis of the results, the authors suggested the following sequence in the enzymatic degradation of phenylalanine and tyrosine: initial deamination to the corresponding acrylic acid derivatives whose side chain is then oxidised with formation of the corresponding C_6-C_1 acids. Further hydroxylation leads to the formation of protocatechuic acid (XXVIII)—the final aromatic compound in the sequence—which then undergoes ring cleavage. The presence of phenyl-lactic and phenylacetic acids in the metabolic products of *S. commune* indicates the existence of yet another pathway, apart from that discussed above, to the degradation of phenylalanine by this organism.

Haider and Flaig [47,119-121] established that, under the influence of *Polystictus versicolor* or the enzyme system isolated from this fungus, protocatechuic acid (XXVIII) is converted into β-oxoadipic acid (XXIX). According to the authors' views, the fungal transformation (XXVIII) → (XXIX) (Scheme 2) proceeds via the same mechanism as the analogous transformation under the influence of bacteria [122-126].

Scheme 2



According to this mechanism, protocatechuic acid oxidase catalyses the initial conversion of protocatechuic acid into *cis*, *cis*-β-carboxymuconic acid (XXX), which can be converted by a number of bacteria under the influence of the specific lactone-forming enzyme into the lactone of β-carboxymuconic acid (XXXI). Both the acid (XXX) and its lactone (XXXI) are then converted into β-oxoadipic acid (XXIX) as a result of the action of two different enzyme systems usually designated as decarboxylase.

Thus the data obtained in the course of the above experiments show that the aromatic ring is cleaved when the compound either contains or can be converted into an *o*- or *p*-dihydroxybenzene derivative. In the microbiological degradation of *o*-dihydroxybenzenes the cleavage can proceed via two different mechanisms. The aromatic ring can be ruptured either between the hydroxy-groups or directly next to a hydroxy-group. *p*-Dihydroxybenzenes undergo ring fission between the carbon atom linked to an OH group and the adjacent carbon atom linked to a substituent [127,128]

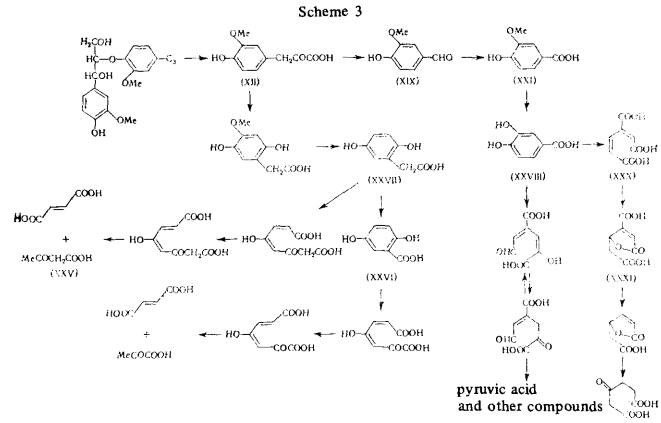
Haider and Grabbe [129] investigated the degradation of labelled biosynthetic [^{14}C] lignin by white rot fungi and concluded that this process probably does not proceed via the initial cleavage of the C–C and C–O bonds in the side chains but involves the fission of the aromatic rings still bound in the polymer. This conclusion did not, however, receive additional experimental confirmation.

Summarising studies on the microbiological degradation of lignin, Haider [48] concluded that the degradation of wood-decomposing fungi involves the following stages without the participation of phenol oxidases: (1) the shortening of the side chain leading to the formation of phenolic aldehydes, which can then be oxidised to the corresponding acids or reduced to the corresponding alcohols; (2) the cleavage of the methyl ether linkages and the elimination of methoxy-groups; (3) the cleavage of aromatic rings.

At the same time phenol oxidases oxidise the lignin decomposition products to coloured polymerisation mixtures. The first stage of this process is dehydrogenation leading to the formation of reactive radicals and quinones.

On the basis of the results of the above investigations, Christman and Oglesby [12] proposed a mechanism for the degradation of the β-aryl guaiacylglyceryl ether linkages in conifer lignin as a result of the action of white rot fungi (Scheme 3).

Scheme 3



Kirk et al. [130] investigated the action of two white rot fungi, *Polyporus versicolor* and *Stereum frustulatum*, on model compounds for lignin: β-guaiacyl guaiacylglycerol ether (VIII) and β-guaiacyl veratrylglyceryl ether (X). Of the two white rot fungi tested, one (*P. versicolor*) is typical and the other (*S. frustulatum*) is atypical. According to the authors [130], these fungi represent extreme varieties of white rot fungi in relation to the formation of phenol oxidising enzymes.

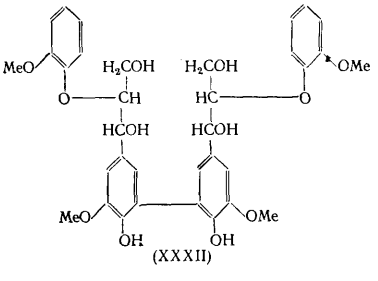
The study established that in the synthetic liquid medium the guaiacyl model (VIII) is converted under the influence of both fungi into a number of products, among which the *oo'*-dihydroxybiphenyl dehydropolymer (XXXII) predominates. This biphenyl derivative was also the main product when compound (VIII) was incubated with laccase. The veratryl model (X) was not changed either by the two fungi tested, in the synthetic aqueous medium, or by purified laccase. However, in a medium containing wood powder compound (X) was oxidised by both fungi to α-guaiacoxy-β-hydroxypropioveratrone (XXXIII). Separate experiments undertaken to elucidate the role of wood powder in this oxidation showed that lignin in wood behaves as a substrate for the formation of radicals when acted upon by the phenol oxidases produced by both fungi.

Thus the fact that β-guaiacyl guaiacylglyceryl ether is susceptible to the action of the white rot fungi tested, while β-guaiacyl veratrylglyceryl ether remains unchanged under the same conditions evidently shows that the phenolic OH group and not the β-ether linkage is involved directly under the above culture conditions. This conclusion is supported also by the finding that β-guaiacyl DL-glyceryl ether is not changed by either of the fungi tested in the synthetic liquid medium. The observed dimerisation of the guaiacyl model to the biphenyl dehydrodimer under the influence of both white rot fungi and the conversion of

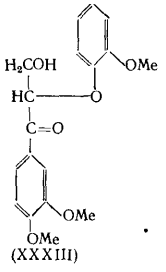
β-guaiacyl veratrylglyceryl ether into the corresponding veratrone in the presence of wood are oxidation reactions and, according to the authors, result from the action of phenol oxidases.

Kirk et al.[94] continued the study of the action of *P. versicolor* and *S. frustulatum* using the β-guaiacyl ether of syringylglycol (XXXIV) as the substrate. The syringyl and not the guaiacyl model was chosen to avoid the condensation reactions catalysed by phenol oxidase, involving the *ortho*-position with respect to the phenolic OH group.

The study established that compound (XXIV) was oxidised by filtrates of the *P. versicolor* culture or by the whole cultures of *S. frustulatum* to α-guaiacoxyacetosyringone (XXXV). Filtrates of the *P. versicolor* culture cleaved the alkyl–phenyl C–C bond in compounds (XXXIV) and (XXXV) with formation of guaiacoxyacetaldehyde (XXXVI) and guaiacoxyacetic acid (XXXVII) respectively.



(XXXII)

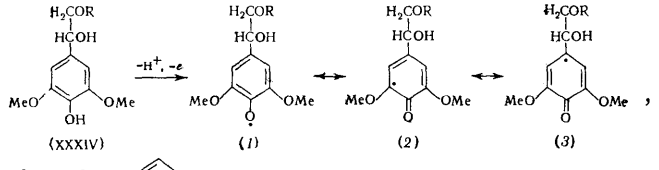


(XXXIII)

The syringyl halve of both initial compounds were converted into 2,6-dimethoxy-*p*-benzoquinone (XXXVIII) by filtrates of *P. versicolor* cultures and whole cultures of *S. frustulatum*. Furthermore it was shown that laccase, isolated from filtrates of *P. versicolor* cultures, catalysed all the above reactions.

At the same time it was established that whole cultures of *P. versicolor* and *S. frustulatum* reduced guaiacoxyacetaldehyde and guaiacoxyacetic acid to 2-guaiacoxyethanol, which accumulated in the reaction medium and was resistant to further changes by any of the above organisms. Since 2-guaiacoxyethanol was formed when whole cultures of both fungi acted on the β-guaiacyl ether of syringylglycol and α-guaiacoxyacetosyringone, the above alkyl–phenyl cleavage can evidently be achieved by whole cultures.

The authors proposed mechanisms for the main reactions occurring in the enzymatic degradation of the model compound (XXXIV). The oxidation of the β-guaiacyl ether of syringyl glycol (XXXIV), catalysed by fungal phenol oxidase, leads to the formation of a free radical, which can exist in at least three main resonance forms. They are analogous to the mesomeric forms R_a, R_c, and R_d of the coniferyl alcohol radical formed, according to Freudenberg's theory[131], during the biosynthesis of lignin.



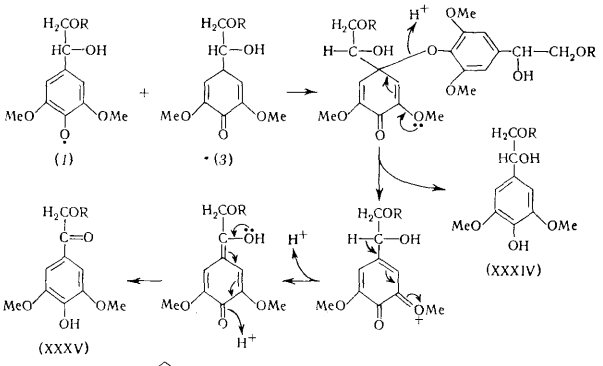
(XXXIV) (1) (2) (3)

where R =

The mesomeric forms of the radical produced can either undergo disproportionation reactions or can recombine to dimeric products, which can then be altered by stabilisation reactions. The formation of biphenyl derivatives by *ortho–ortho* coupling [including the radical form (2)], observed for guaiacyl compounds[94,132,133], is limited to a large extent by the methoxy-groups in the syringyl compounds, i.e. the fraction of the radicals in form (2) is insignificant in the subsequent reactions[134,135].

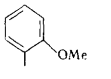
The mechanism of the oxidation of the β-guaiacyl ether of syringylglycol, which constitutes essentially a disproportionation reaction, is presented in Scheme 4.

Scheme 4



(1) (3) (XXXIV) (XXXV)

where R =



The initial stage of the above process involves the coupling of the phenoxyl (1) and the methylenequinonoid (3) radical forms. The distribution of the electron pair of the methoxyl oxygen atom over the cyclohexadienone ring leads to the elimination of a molecule of the β-guaiacyl ether of syringylglycol (XXXIV). Subsequent stabilisation of the molecule formed is achieved by the loss of a proton from the benzyl carbon atom. Rearomatisation leads to the formation of α-guaiacoxyacetosyringone (XXXV).

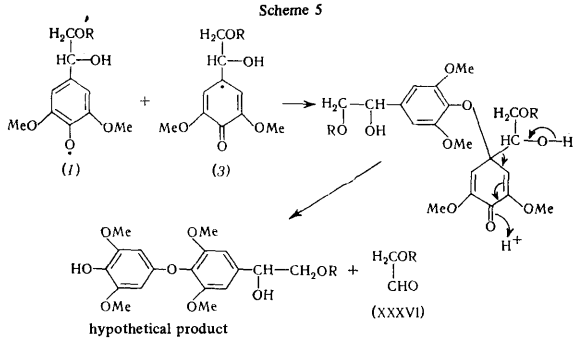
Scheme 5 presents the mechanism for the formation of guaiacoxyacetaldehyde (XXXVI) from the β-guaiacyl ether of syringylglycol.

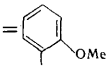
The initial coupling of the radicals in the mesomeric forms (1) and (3) is followed by the transfer of a proton from the benzyl OH group to the *p*-methylenequinonoid half. The subsequent cleavage of the benzyl–ring C–C bond liberates the side chain in the form of the aldehyde and leads to the rearomatisation of the initial molecule.

There is also a possibility of the coupling of two radicals in the mesomeric form (3). The dehydrodimer formed yields 3,3′,5,5′-tetramethoxy-*p*-biphenyl, as a result of the elimination of both side chains, which is converted on further oxidation into cerulignone. The latter was detected in very small amounts by Kirk et al.[94] in the products of the oxidation of model compound (XXXIV) by laccase from *P. versicolor*. However, this reaction is apparently limited by steric hindrance.

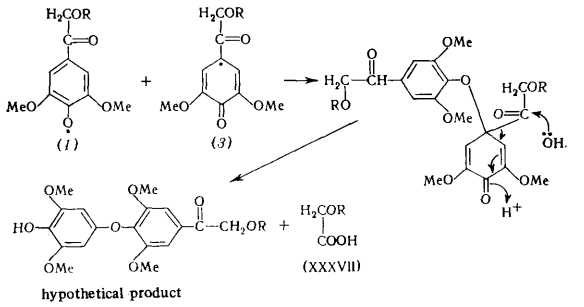
A similar mechanism (see Scheme 6) was proposed to account for the formation of guaiacoxyacetic acid (XXXVII) from α-guaiacoxyacetosyringone (XXXV).

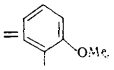
Scheme 5



where R = 

Scheme 6

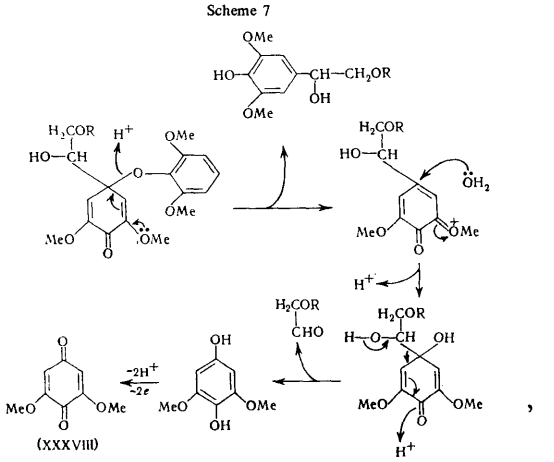


where R = 

After the coupling of the phenoxyl (1) and *p*-methylenequinonoid (3) forms of the radical, produced as a result of the oxidation of the phenol, nucleophilic attack by a water molecule on the carbonyl substituent in the cyclohexadienone ring leads to its migration, yielding guaiacoxyacetic acid (XXXVII) and diphenyl ether. There is a possibility of the recombination of two *p*-methylenequinonoid radicals in form (3) with subsequent elimination of both side chains; this leads to the formation of 3,3′,5,5′-tetramethoxy-*p*-biphenyl, which is then oxidised to cerulignone. The later was obtained in a very small yield in the oxidation of compound (XXXV) by laccase from *P. versicolor*.

The formation of 2,6-dimethoxy-*p*-benzoquinone (XXXVIII) by the oxidative cleavage of the β-guaiacyl ether of syringylglycol is illustrated in Scheme 7.

Scheme 7



where R =

The initial stage in this process is also the coupling of the phenoxyl and *p*-methylenequinonoid forms of the radical, leading to an unstable cyclohexadienone derivative (this stage is not included in Scheme 7). The distribution of the electron pair of one of the methoxyl oxygen atoms over the cyclohexadienone ring leads to the elimination of a molecule of the β-guaiacyl ether of syringylglycol. Next, there is nucleophilic attack by water on the 4-position of the cyclohexadienone ring with subsequent loss of the proton. The elimination of guaiacoxyacetaldehyde with rearomatisation of the dienone half yields 2,6-dimethoxyhydroquinone, which is oxidised enzymatically to the corresponding *p*-quinone. A similar mechanism can account for the formation of a quinone from two molecules of α-guaiacoxyacetosyringone.

On the basis of the results of these investigations, Kirk, Harkin, and Cowling put forward the so called "phenol oxidase" hypothesis to account for the mechanism of the depolymerisation of lignin by white rot fungi. According to this hypothesis, the phenol oxidising enzymes present in the hyphae of the white rot fungi, and probably liberated from them when the latter penetrate the woody tissue, catalyse the oxidation of the phenolic OH groups in the lignin macromolecule. The resulting unstable free radicals are then stabilised by reactions which condense certain lignin structures but at the same time lead to the cleavage of the carbon–carbon bonds between the side chains and the rings of other oxidised phenylpropanoid units. The subsequent elimination of the terminal aliphatic component exposes additional phenolic OH groups to continuing degradation by enzymatic oxidation. The overall effect of these processes should theoretically lead to fragments of certain components of the lignin macromolecule and to the condensation of the residue.

It is interesting to note that the alkyl–phenyl cleavage reactions on which the proposed hypothesis is based, were first observed in the course of detailed studies on the biosynthesis of lignin. In particular, Freudenberg et al.[136] showed that in the enzymatic dehydogenation of sinapyl alcohol its condensation stops at the syringaresinol dimer and that the continuing enzyme action led to the breakdown of the dimer. The detection among the degradation products of 2,6-dimethoxy-*p*-benzoquinone is evidence that the oxidative dissociation of the alkyl–aryl carbon–carbon bonds took place. Furthermore, the authors reported that, when the oxidation of lignin by purified laccase is continued, 2-methoxy-*p*-benzoquinone is formed.

Structural elements of a new important type—the 1,2-diarylpropane-1,3-diol structures—were detected in lignin comparatively recently[137–139]. The mechanism of their formation in the enzymatic dehydrogenation of *p*-hydroxycinnamyl alcohols, proposed by Lundquist and Miksche[137], involves the alkyl–phenyl cleavage. Subsequently additional experimental confirmation was obtained for this mechanism[139,140]. Finally, in the course of a study of the products of the enzymatic dehydrogenation of propioguaiacone, Pew and Connors[141] identified a triphenyl derivative, the formation of which involves in all probability the cleavage of the alkyl–phenyl bond.

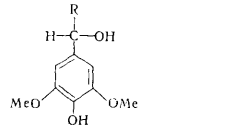
On the basis of the schematic formula of the fragment of the lignin molecule proposed by Freudenberg[131,142], Kirk et al.[94] calculated that 41% of the phenylpropane units of lignin are sensitive to the types of cleavage described above.

In order to elucidate the role of peroxidase and laccase in the degradation of lignin, Gierer and Opara [143] investigated the action of these enzymes on monomeric (guaiacol, 2,6-dimethoxyphenol, and aryl glyceryl ethers) and dimeric (1-guaiacyl-2-syringylethanol, pinoresinol, and dihydrodehydrodi-isoeugenol) phenolic compounds structurally related to lignin. The enzyme action led to the formation of products of a higher molecular weight, as a result of carbon–carbon and carbon–oxygen coupling. Non-phenolic model compounds were not involved by either enzyme system. This is evidence that their catalytic effect is oxidative and not hydrolytic.

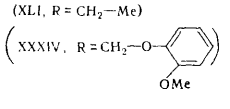
The results of the above study showed that both enzyme systems function mainly if not exclusively by catalysing oxidative coupling with formation of aryl–aryl or aryl–O–aryl bonds. No evidence was obtained for the cleavage of the ether linkages—the coupling products contained all the alkyl–aryl bonds present initially, including the aryl methyl and β-alkyl aryl ether linkages. Thus the degrading effect of the enzymes must be related to the oxidative coupling reactions which they catalyse. Such dehydrogenation reactions, which model compounds of p-hydroxy-α-carbonyl [94,144] and p-hydroxy-α-carbonyl [94,145] types are caused to undergo by laccase [94] or peroxidase [144,145], were examined above.

The identical compositions of the coupling products obtained with peroxidase–H_2O_2 and with laccase and the lack of substrate specificity in both enzymes are evidence that only the first stage of these reactions—the abstraction of hydrogen from the phenolic hydroxyl—are catalysed by the enzymes. The subsequent couplings evidently take place spontaneously. The authors point out that in the course of the above investigation no experimental evidence was obtained for the direct involvement of either enzyme in the microbiological degradation of lignin. However, this does not rule out the possibility that the oxidative coupling reaction can constitute the first step in the reaction sequence where peroxidase and laccase are involved in the microbiological cleavage of lignin in combination with other still unknown enzymes.

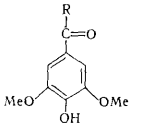
As mentioned above, Kirk and coworkers, who investigated the enzymatic degradation of a number of lignin model compounds, suggested the existence of free-radical intermediate compounds, which might arise as a result of the loss of one electron from the corresponding phenols. Furthermore, it has been noted that decayed wood is characterised, according to ESR data, by a higher free radical concentration [75–77]. In order to establish which lignin structures form the most stable types of free radicals in enzymatic degradation, Caldwell and Steelink [79] oxidised a number of syringyl derivatives, including the benzyl alcohols (XXXIX)–(XLI) and (XXXIV), the α-carbonyl compounds (XLII)–(XLIV) and (XXXV), syringylpropane (XLV), and syringaresinol (XLVI) with H_2O_2 in the presence of horseradish peroxidase and established that these compounds give rise to stable intermediate phenoxy-radicals.



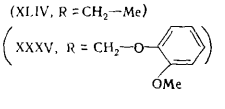
(XXXIX, R = H)
(XL, R = Me)
(XLI, R = CH_2–Me)



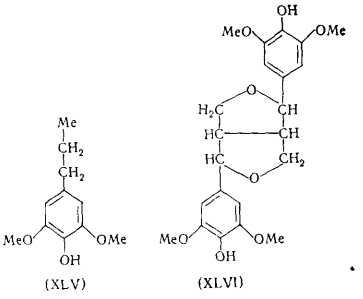
(XXXIV, R = CH_2–O–)



(XLII, R = H)
(XLIII, R = Me)
(XLIV, R = CH_2–Me)



(XXXV, R = CH_2–O–)

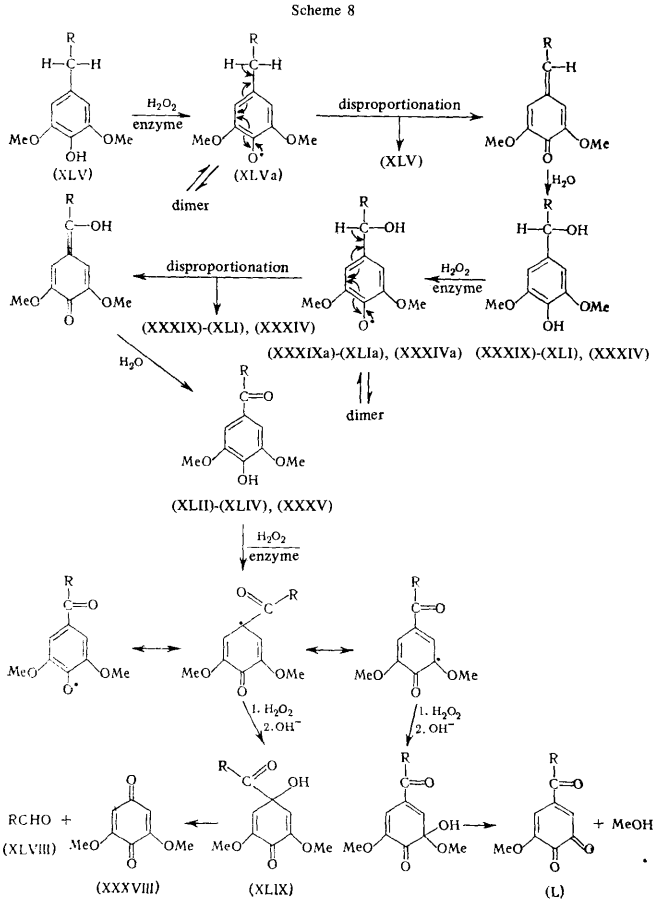


(XLV) (XLVI)

The results of these investigations showed that the phenoxy-radicals are formed most readily from α-carbonyl syringyl derivatives, less readily from α-carbinol, and α-alkyl ether derivatives, and slowly from alkyl derivatives.

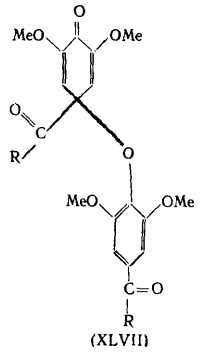
In order to establish the sequence of the reactions occurring in the oxidation of the compounds tested, the reaction mixture was examined simultaneously by ESR and optical spectroscopy. In addition, aliquots of the reaction mixture were periodically subjected to thin layer chromatographic separation in order to identify the reaction products. The mechanism proposed for the enzymatic oxidation of the compounds investigated on the basis of the results is presented in Scheme 8.

Scheme 8



The peroxidase–H_2O_2 system probably abstracts the phenolic hydrogen atom from the substrate. The resulting phenoxy-radical, which is in equilibrium with the hydroquinone-ether dimer (XLVII), then disproportionates, yielding a phenol with a higher oxidation potential. This

second phenol does not undergo further oxidation until the entire initial substrate is used up. This process is repeated until the side chain is split off.



(XLVII)

Thus enzymatic oxidation proceeds via a sequence of separate stages. The abstraction of the hydrogen atom probably determines the rate of reaction in each change of the oxidation state of the substrate. The disproportionation of two radical forms (or a dimeric form) is rapid.

It is noteworthy that Pew [132] reported earlier that H_2O_2 and peroxidase are capable of hydroxylating the α-position of syringylpropane. Caldwell and Steelink showed that this reaction is also a one-electron transfer process. The reaction of peroxidase and H_2O_2 with compound (XXXIV), which the authors investigated, is of special interest. The oxidation of this compound by laccase was studied in detail by Kirk et al. [130], who showed that the main product is compound (XXXV) with additional formation of a certain amount of (XXXVI), (XXXVIII), and of unidentified products. The high yield of compound (XXXV) is probably due to its insolubility in water, which prevented its further oxidation. Since Caldwell and Steelink oxidised compound (XXXIV) in a water–methanol medium, in which compound (XXXV) dissolved, they obtained a high yield of the phenoxy-radical from (XXXV) and of compound (XXXVIII).

According to Scheme 8, the quinone (XXXVIII) and the aldehyde (XLVIII) are formed in the last oxidation stage. Caldwell and Steelink suggested two possible ways for the decomposition of the radicals formed from compounds (XLII)–(XLIV) and (XXXV)—via the intermediate (XLIX) or its hyperoxide precursor, which can yield directly compounds (XXXVIII) and (XLVIII), and also via the *o*-quinone (L), which can be a source of a small amount of an unidentified red substance.

Later Young and Steelink [146] established that, when horseradish peroxidase and H_2O_2 are allowed to act on 4-substituted 2,6-dimethoxyphenols and also MWL and alkaline lignins from the wood of deciduous trees, phenoxy-radicals are formed, the lignin substrates being degraded by the same oxidation mechanism as the simple phenolic substrates.

The results of the above studies suggest that the α-carbonyl groups in units with a free phenolic hydroxyl are most sensitive to the fungal attack on the lignin macromolecule. If the decomposition of all the lignin units with a free phenolic hydroxyl proceeds via the free-radical mechanism proposed by Caldwell and Steelink, then this can explain the appreciable depolymerisation of lignin on the basis of a series of one-electron hydrogen abstraction steps. On the other hand, one must emphasise [147] that the main dehydrogenation stage is regulated by the structure of the phenolic substrate and also by the oxidation potential of the enzyme or the chemical oxidant. In biological systems the possibility of such oxidation depends largely on factors such as the presence of the appropriate enzymes, the pH of the medium, and the presence of oxidants, for example O_2 or H_2O_2. The combination of these factors determines the preferential occurrence and extent of the polymerisation or degradation reactions under the influence of the same enzyme–oxidant system.

Sergeeva and coworkers [148] investigated the action of the brown rot fungus *Fomitopsis pinicola* I on coniferin, glucovanillin, vanillin, syringaldehyde, and coniferyl alcohol. Syringaldehyde and vanillin did not undergo any changes as a result of the enzyme action, while coniferyl alcohol was oxidised to vanillin. The action of the fungus *F. pinicola* I on coniferin and glucovanillin led to the dissociation of the β-phenylglucosidic linkage with formation of coniferyl alcohol and vanillin respectively. These primary decomposition products underwent further oxidation. Thus vanillic acid and a further two unidentified acids were detected together with vanillin in the products of the decomposition of glucovanillin after exposure to the action of the fungus for 10 days. Coniferyl alcohol and coniferaldehyde were detected in the coniferin decomposition products after 10 days, and after more prolonged enzyme action (45 days) vanillin was found as well.

The authors suggest that coniferyl alcohol is formed from coniferin and vanillin is formed from glucovanillin under the influence of the fungus *F. pinicola* I via an intermediate stage involving the formation of unstable phenoxy-radicals. The hypothesis has been put forward, that when *F. pinicola* I acts on wood, the dissociation of β-phenyl-glucosidic lignocarbohydrate linkages can lead to the formation of stable phenoxy-radicals. The subsequent oxidation of coniferyl alcohol to coniferaldehyde and of coniferaldehyde to vanillin also evidently proceeds via free-radical intermediates. The authors believe that the abrupt increase in the concentration of paramagnetic centres observed on extensive enzymatic decomposition of wood [77] may be a consequence of the oxidation of the lignin structures and the formation of stable phenoxy-radicals. On the basis of the content of functional groups and the infrared spectroscopic data for sprucewood and birchwood obtained in the course of successive stages of their degradation by *F. pinicola* I, Kreitsberg and coworkers [149,150] concluded that the number of quinhydrone structures in the lignin macromolecule increases, the biolignin isolated from degraded sprucewood containing more of these structures than the analogous preparation from birchwood.

In conclusion of the discussion of the possible pathways in the microbiological degradations of lignin, certain general comments have to be made. As already mentioned, there is evidence for the presence in the wood decomposing fungi of an enzyme system capable of cleaving β-aryl arylglyceryl ether linkages in lignin. However, the dissociation of these bonds does not evidently lead to the liberation of appreciable amounts of monomeric products, although it can cause the depolymerisation of lignin.

For this reason the so called "phenol oxidase hypothesis", put forward by Kirk, according to which the phenol oxidising enzymes of the wood decomposing fungi catalyse the oxidation of the phenolic OH group of the lignin macromolecule, appears to have more justification. As a result, unstable free radicals are formed and are then stabilised in the course of reactions leading to the condensation of certain lignin structures and the simultaneous cleavage of carbon–carbon bonds between the side chains and rings of other oxidised phenylpropane units. According to Caldwell and Steelink, the degradation of lignin takes

place as a result of a series of one-electron transfer processes leading ultimately to the removal of the side chains.

One should bear in mind that, in consequence of the wide variety of linkages between the monomeric units in lignin [151], its complete decomposition may not involve a direct attack on each linkage with the resulting liberation of low-molecular-weight compounds. Direct attack on the general structural elements of the polymer, such as aromatic rings, is more likely and the dissociation of the linkages between the phenylpropane units may take place indirectly. However, the available data are inadequate to reach definite conclusions.

Thus the studies examined in the present review do not unfortunately permit an unambiguous conclusion either about the enzyme systems present in wood-decomposing fungi or about the mechanism of the microbiological degradation of lignin, although the solution of these problems is evidently necessary for successful research in the fields of study discussed in the introduction.

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Free Radicals Derived from Phosphorus Compounds

V.V.Pen'kovskii

Studies on phosphorus-containing free radicals and radical-ions are discussed in the review and data on the geometrical and electronic structures of phosphinyl, phosphonyl, and phosphoranyl radicals and radical-ions derived from compounds of tri-, tetra-, and penta-coordinate phosphorus are presented. The main types of radical reactions of phosphorus and their mechanisms are considered.
The bibliography includes 225 references.

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I. INTRODUCTION

The autoxidation of white phosphorus, the process to which phosphorus owes its name, proceeds via a branched radical-chain mechanism[1]. The autoxidation of phosphine is also a radical-chain reaction[2]. Nevertheless free radicals derived from phosphorus compounds remained little studied for a long time, since in the first stages of the development of phosphorus chemistry investigators concentrated their attention on the study of heterolytic reactions. In 1945 Kharasch et al.[3] established that free radicals are involved in the reaction of PCl_3 with oct-1-ene; somewhat later a free-radical mechanism was proposed by Soborovskii et al.[4] for the joint oxidation of PCl_3 and hydrocarbons. At the beginning of the 1960s many reactions of phosphorus compounds were regarded as having a free-radical mechanism[5,6].

In 1961 Horsfield et al.[7] detected by ESR the $\dot{P}O_3^{2-}$ radical-ion on γ-irradiation of $Na_2HPO_3.5H_2O$ crystals. Subsequently numerous phosphorus-containing free radicals were detected by ESR and it was shown that their formation is indeed an intermediate stage in a number of reactions. At present the study of free radicals derived from phosphorus compounds and of their role in chemical reactions is being prosecuted vigorously and on a large scale.

Free radicals derived from phosphorus compounds can be divided into three groups: phosphinyl ($R_2\dot{P}$), phosphonyl ($R_2\dot{P}O$), and phosphoranyl ($R_4\dot{P}$). The aminyl and iminoxy- or nitroxy-radicals correspond to the first and second

groups respectively, while the third group has no analogues among nitrogen radicals. Furthermore, radical-cations derived from phosphines ($R_3P^{\cdot+}$) and their derivatives and also radical-anions containing tri- or tetra-coordinate phosphorus are known. The properties of the radical-anions of tri-coordinate phosphorus resemble those of phosphonyl radicals and those of tetra-coordinate phosphorus resemble the properties of phosphoranyl radicals.

II. PHOSPHINYL RADICALS

1. Generation

Phosphinyl radicals can be generated by the homolytic dissociation of the P–X bond on heating, irradiation, or abstraction of the substituent X by another radical. For example, $\dot{P}F_2$ radicals are generated on irradiation of ND_4PF_6 with γ-rays[8], on irradiation of PF_3 with electrons in a sulphur hexafluoride[9] or xenon hexafluoride (XeF_6)[10] matrix, on thermal dissociation of P_2F_4 and PF_2H [11,12] (they cannot be obtained on heating PF_3), and on ultraviolet irradiation of PF_2H in an argon matrix[12]. $\dot{P}Cl_2$ radicals were obtained by the ultraviolet irradiation of PCl_3 at −196°C [13], the condensation of PCl_3 or PBr_3 and lithium vapours in argon at −258°C yielded $\dot{P}Cl_2$ and $\dot{P}Br_2$ radicals [14], and $\dot{P}I_2$ radicals were produced by the photolysis of P_2I_4 and PI_3 in hexane or cyclohexane[15].

The simplest phosphinyl radical $\dot{P}H_2$ was identified by flash photolysis [16,17], $\dot{P}F_2$ was identified by mass spectrometry[18], and $\dot{P}Cl_2$ was identified by infrared spectroscopy[14]. All these radicals and many other phosphinyl radicals were also studied by ESR [8–10,12,19–22]; the parameters of their ESR spectra are presented in Table 1. Phosphinyl radicals with alkyl groups at the phosphorus atom have not so far been detected by any physical method.

2. Structure

The unpaired electron in the $\dot{P}H_2$ radical is in the *p* orbital of phosphorus at right angles to the plane of the bonds; the ground state[17] of the radical is $^2B_1$ and its electronic configuration is $KL\,(1a_1)^2\,(1b_2)^2\,(2a_1)^2\,(1b_1)^1$. The unpaired electron in $\dot{P}F_2$ is also in similar *p* orbitals of phosphorus and fluorine; these are typical π-electron radicals. According to the most reliable data[10], the values of a_P for both radicals are almost the same (Table 1). Therefore the delocalisation of the unpaired electron in $\dot{P}F_2$ should be small and the observed slight splitting by ^1H and ^{19}F nuclei is due to the σ–π interaction. $\dot{P}Cl_2$ radicals should have analogous properties. The ESR spectra of PBr_2 and $\dot{P}I_2$ have not been studied.

The infrared spectra of $\dot{P}Cl_2$ and $\dot{P}Br_2$ have shown[14] that these radicals are non-linear; according to the calculation of the normal vibrations, the valence angle in both radicals is close to 120° and the force constants of the P–X bond are approximately the same as for PCl_3 and PBr_3 molecules. Thus in these cases too the stabilisation of the radical by the delocalisation of the unpaired electron over the halogen atom should be small.

Kilcast and Thomson[23] calculated the equilibrium geometry and the distribution of spin density in the simplest phosphorus radicals by the unrestricted Hartree–Fock method in terms of the CNDC/2 approximation; the valence angles and bond lengths were found by minimising the total energy. The results of the calculation on phosphinyl radicals are presented in Table 2. As was to be expected, the spin density in $\dot{P}F_2$ and $\dot{P}Cl_2$ is concentrated mainly in the phosphorus *p* orbital. Accordingly the electrons involved in the formation of bonds are appreciably displaced towards the ligand atoms; for example, the charges on the fluorine atoms are −0.26. Owing to the repulsion of these charges, the valence angle in $\dot{P}F_2$ is greater than in $\dot{P}H_2$. The bonds are elongated compared with the initial phosphines. Comparison of the calculation[23] with experimental ESR data showed that the values of a_P found previously[8,12] were erroneous. A non-empirical calculation on $\dot{P}F_2$ with inclusion of the 3*s* and 3*p* orbitals of fluorine and the 3*d*, 4*s*, and 4*p* orbitals of phosphorus in the basis set confirmed this conclusion[24]. The equilibrium geometry of $\dot{P}Cl_2$ calculated by Kilcast and Thomson[23] is not entirely reliable, since it does not apparently correspond to the true total energy minimum.

Table 1. Parameters of the ESR spectra of phosphinyl radicals.

Radical	*g*-Factor	Type of splitting	Isotropic splitting constants, G		References
			a_P	a_X	
$\dot{P}H_2$	2.0087	2×3	80	18	19
$\dot{P}F_2$	2.0108	2×3	36	60.5	8
	1.9952	2×3	47	65	12
	2.0020	2×3	84.6	32.6	10
$\dot{P}Cl_2$	2.014	2×7	71	5	13
$\dot{P}HPh$		2	251		20
$\dot{P}Ph_2$	2.0036	2×4	12.0	5.8	21
$\dot{P}(OEt)_2$	2.002	2	78.5		22

Table 2. The distribution of spin densities and equilibrium structures of phosphinyl radicals.

Radical	Spin density at the $3p_\pi$ atomic orbital of phosphorus	∠XPX	R_{PX}, Å
$\dot{P}H_2$	1.000	91.5° *	1.52
$\dot{P}F_2$	0.937	112°	1.73
$\dot{P}Cl_2$	0.718	140°	1.95

*Experiment[17]: ∠HPH = 91.7°, R_{PH} = 1.429 Å.

The $Ph\dot{P}H$ radical is distinguished by an exceptionally high constant a_P, but the reasons for this anomaly have not been elucidated. The lower value of a_P for $\dot{P}Ph_2$ is due to the delocalisation of the spin density over the radical. Wong and Wan[21] suggest that it is delocalised only over one benzene ring, where the protons in the *ortho*- and *para*-positions are equivalent; however, this interpretation of the observed spectrum is fairly controversial.

3. Reactions of Phosphinyl Radicals

All phosphinyl radicals, particularly those containing alkyl groups, are very unstable. Pellon[25], who determined the chain transfer rate constants for phosphinyl radicals in the polymerisation reactions of styrene and methyl methacrylate, established the following stability series for phosphinyl radicals: $Ph\dot{P}H > (NCCH_2CH_2)_2\dot{P} > C_8H_{17}\dot{P}H \simeq NCCH_2CH_2\dot{P}H$.

Two types of reactions are characteristic of phosphinyl radicals: (1) the abstraction of an atom from an adjacent neutral molecule; (2) addition to a double bond.

Reactions involving the abstraction of an atom (usually a hydrogen atom) normally take place when the radical interacts with the solvent, for example in the photolysis of triphenylphosphine in benzene in an atmosphere of nitrogen [26]:

$$Ph_3P \xrightarrow{h\nu} Ph_2\dot{P} + Ph^{\cdot} , \quad (1)$$

$$Ph_2\dot{P} + C_6H_6 \rightarrow Ph_2PH + Ph^{\cdot} . \quad (2)$$

Various mechanisms have been proposed for the reactions of $\dot{P}Ph_2$ with alcohols [26-28]. Wong et al. [29] established that they too involve the abstraction of a hydrogen atom from the α-carbon atom of the alcohol molecule (but not from the hydroxy-group, as shown in experiments with MeOD). Diphenylphosphine is partly oxidised to diphenylphosphine oxide. The data concerning the presence of alkyldiphenylphosphine [26] and phosphonium salts [27] in the reaction products were not confirmed [29].

Reactions involving the addition of phosphinyl radicals to double bonds are commonest and have been most thoroughly investigated. For example, $\dot{P}H_2$ reacts with olefins on ultraviolet irradiation or on heating to 80–100° of a mixture of PH_3, the olefin, and benzoyl peroxide [5]:

$$\dot{P}H_2 + R_2C{=}CH_2 \rightarrow H_2PCH_2\dot{C}R_2 . \quad (3)$$

The resulting radical reacts with another PH_3 molecule:

$$H_2PCH_2\dot{C}R_2 + PH_3 \rightarrow H_2PCH_2CHR_2 + \dot{P}H_2 . \quad (4)$$

The phosphine molecule can then give rise to the radical $H\dot{P}CH_2CHR_2$, which also adds to the olefin molecule; the reaction products are a mixture of primary, secondary, and tertiary phosphines. The addition reaction of phosphinyl radicals is reversible, since but-2-ene undergoes *cis–trans* isomerisation in the presence of $PhPH_2$, $n\text{-}Bu_2PH$, and $PH_2CH_2CH_2CN$, and azobisisobutyronitrile at 70°C. [30]

The reactions of PH_3, $PH_2CH_2CH_2CN$, and $PH(CH_2CH_2.CN)_2$ with cyclohexane [31], of phenylphosphine with allylamine, allyl acetate, and 2-methyl-5-vinylpyridine [32], and of PH_3 with fluoroolefins [33] proceed similarly, the phosphinyl radical always adding to the least substituted carbon atom. A kinetic study [34] of the reaction of tetrafluoroethylene with an excess of dimethylphosphine in the gas phase at 212–288°C showed that it is initiated by the bimolecular abstraction of a hydrogen atom from the dimethylphosphine molecule and proceeds subsequently via a free-radical chain mechanism in accordance with reactions (3) and (4); chain termination takes place as a result of the recombination of the dimethylphosphinyl radicals.

If the initial phosphine is unsaturated, the addition of phosphinyl radicals to a double bond can be modified; its products are telomers and polymers with phosphorus atoms in the chain. For example, phenylallylphosphine polymerises in this way on ultraviolet irradiation [5].

The mechanism of the reactions of PCl_3 with olefins should be analogous in principle [3]. In reality the yield of the products of the addition $\dot{P}Cl_2$ to olefins is low; high-boiling products are formed [35]. The reaction probably proceeds mainly via a different mechanism (see Section IV). The difference in the behaviour of $\dot{P}H_2$($\dot{P}Alk_2$, $Ar\dot{P}H$) and $\dot{P}Cl_2$ is probably due to the fact that the process involving the dissociation of the P–H bond and the addition of $\dot{P}H_2$ is exothermic (the dissociation of the P–H bond instead of C–H results in an energy gain of about 13 kcal $mole^{-1}$), while the corresponding reaction of PCl_3 is thermally neutral [5]. These considerations are confirmed by the absence of $\dot{P}F_2$ radicals in the thermolysis of PF_3. [12]

Phosphinyl radicals can also add to the C=N bond; the reaction of diethylphosphine and diphenylphosphine with isonitriles (in the presence of azobisisobutyronitrile as an initiator) is known [36]:

$$R_2\dot{P} + R'N{=}C \rightarrow R_2P\dot{C}{=}NR' \xrightarrow{} R_2PC{\equiv}N + \dot{R}' , \quad (5)$$

$$R_2\dot{P} + R'N{=}C \rightarrow R_2P\dot{C}{=}NR' \xrightarrow{R_2PH} R_2PCH{=}NR' + R_2\dot{P} . \quad (6)$$

Pathway (5) is preferred when R′ = CH_2PH or t-Bu and pathway (6) is preferred when R′ is another alkyl radical.

Finally, phosphinyl radicals can add to triple carbon–carbon bonds; for example, $PH_2CH_2CH_2CN$ and $PH(CH_2.CH_2CN)_2$ interact with hept-1-yne via a radical mechanism [32].

III. PHOSPHONYL RADICALS

1. Generation

The $(MeO)_2\dot{P}O$ and $(EtO)_2\dot{P}O$ radicals were detected by ESR on irradiation of single crystals of dimethyl and diethyl phosphites with X-rays [37]; in this case the main process is selective homolysis, so that only two types of radicals, uniformly distributed in the crystal, are formed. $(EtO)_2\dot{P}O$ can also be generated by the ultraviolet irradiation of triethyl phosphite at −196°C. Initially there is a homolytic dissociation of the O–C bond with formation of the $(EtO)_2\dot{P}O$ radical, which is then converted into $(EtO)_2PO$. [38]

Davies et al. [39] obtained $(RO)_2\dot{P}O$ radicals (R = Me, Et, i-Pr, or n-Bu) by the ultraviolet irradiation of solutions of the corresponding phosphites and di-t-butyl peroxide. When phosphites are treated with $TiCl_3 + H_2O_2$, products of the dissociation of the C–H bond in one of the alkyl groups are obtained instead of phosphinyl radicals. Thus the dissociation of the C–H bond is slower than the dissociation of the P–H bond.

The phosphinyl radicals $(MeO)_2\dot{P}O$ are also formed in the low temperature γ-irradiation of trimethyl phosphate [40], probably in consequence of the elimination of the MeO^- anion from the primary $(MeO)_3PO^{\cdot-}$ radical-anion (see Section VII). The $\dot{P}OCl_2$ radical was detected by ESR in γ-irradiated $POCl_3$ [41] and the $Ph_2\dot{P}O$ (Geoffroy and Lucken [42]) and $Me_2\dot{P}O$ (Begum and Symons [43]) radicals were detected in irradiated diphenylphosphinous acid and trimethylphosphine oxide respectively.

2. Structure

Table 3 lists the g-factors for phosphonyl radicals, the ^{31}P hyperfine splittings, and the spin densities ρ_S and ρ_p in the 3s and 3p orbitals of phosphorus. Evidently the latter are fairly large, so that the unpaired electron is not localised at the oxygen atom; this is confirmed by the difference between the ESR spectra of the $(EtO)_2\dot{P}O$ and $(EtO)_2\dot{P}O$ radicals [39]. With the exception of $Me_2\dot{P}O$ in the solid phase, splitting by protons is not observed, although the spin density in the $Ph_2\dot{P}O$ radical is undoubtedly delocalised over the benzene rings. The numerical values lead to the conclusion that the phosphonyl radicals are non-planar [37,42], but more accurate information about their structures is not available in the literature.

Chemical polarisation of ^{31}P nuclei was observed for the first time in the reaction of the t-BuO· and BzO· radicals with dialkyl phosphites [44]. This phenomenon was used as a method for the investigation of the generation and subsequent reactions of phosphonyl radicals derived from alkyl phosphites in the thermal decomposition of dicyclohexyl peroxydicarbonate (DCP) and dilauryl peroxide (DLP) [45-48], in the thermal decomposition of di-t-butyl peroxide [45,47], and in the ultraviolet photolysis of aldehydes and ketones [44,46] or phenylazotriphenylmethane [47]. Phosphonyl radicals are formed in all these reactions as a result of the abstraction of a hydrogen atom from the phosphite molecule; the hypothesis of the "adhesion" of the radicals derived from DCP and DLP to P=O bonds and the formation of radicals of the type $(RO)Ph(OMe)_2\dot{O}$, put forward by Pobedimskii et al. [46], was disproved by Levin et al. [47] In the ultraviolet photolysis of phenylazotriphenylmethane phosphonyl radicals recombine with phenyl and triphenylmethyl radicals into singlet radical pairs with formation of phosphonates [47]; other reactions proceed similarly [45,47]. Chemical polarisation of ^{31}P nuclei in the reaction products of phosphonyl radicals released from cages was observed in the thermal decomposition of benzoyl peroxide in the presence of 2,2,6,6-tetramethylpiperidine *N*-oxide or toluene [45]. The reaction of dimethyl phosphite with peroxides is of quasifirst order; the activation energies for the reactions with DCP and DLP are 29.5 and 33 kcal mole^{-1} respectively [48].

Table 3. Parameters of the ESR spectra of phosphonyl radicals.

Radical	g-Factor	$a_{iso}(^{31}P)$, G	ρ_s	ρ_p/ρ_s	References
$(MeO)_2\dot{P}O$		684	0.188	2.86	37
	2.004	700	0.192		39
	2.005	691	0.190		40
$(EtO)_2\dot{P}O$		671	0.184	2.98	37
	2.032	762	0.209		38
	2.005	687	0.189		39
$(EtO)_2P'O'$	2.021	445	0.122		38
$(i\text{-}PrO)_2\dot{P}O$	2.004	685	0.188		39
$(n\text{-}BuO)_2\dot{P}O$	2.005	688	0.189		39
$Cl_2\dot{P}O$	2.002	759*	0.209	1.6	41
$Ph_2\dot{P}O$	2.0036	390	0.107	5.6	42
$Me_2\dot{P}O$	2.005	375**	0.103	7.6	43

*$a_{iso}(^{35}Cl) = 18$ G.
**at −196°C; $a_H = 19$ G.

Phosphonyl radicals are relatively stable between −50° and −10°C. The reaction involving the abstraction of an atom from neighbouring molecules is apparently more characteristic of these species than of phosphinyl radicals. For example, at −28° they readily abstract the bromine atom from EtBr, t-BuBr, $PhCH_2Br$, and $CH_2=CHCH_2Br$, without adding to the double bond in the last case; the abstraction of a Cl atom proceeds with greater difficulty and is observed only for t-BuCl. In all cases the abstraction of a halogen was confirmed by ESR spectroscopy of the corresponding alkyl radicals [39]. Phosphonyl radicals can also abstract a hydrogen atom from the molecule of the initial phosphite, initiating a radical-chain reaction, but this process is slower than the abstraction of a bromine atom.

Phosphonyl radicals add to olefins in a manner resembling the addition of phosphinyl radicals [49,50]:

$$(RO)_2P(O)H + \dot{R}'' \rightarrow (RO)_2\dot{P}O + R''H \quad , \qquad (7a)$$

$$(RO)_2\dot{P}O + R'CH{=}CH_2 \rightarrow (RO)_2P(O)CH_2\dot{C}HR' \quad , \qquad (7b)$$

$$(RO)_2P(O)CH_2\dot{C}HR' + (RO)_2P(O)H \rightarrow (RO)_2P(O)CH_2CH_2R' + (RO)_2\dot{P}O. \qquad (7c)$$

The reactions proceed at 100–110°C in 55–75% yields [5]. The addition of phosphonyl radicals to acetylenes [51] and unsaturated silanes [52] has been described. The polymerisation of the monobutyl ester of vinylphosphinous acid also proceeds with participation of phosphonyl radicals, since it is initiated by azobisisobutyronitrile or heat and the infrared spectra indicate a heterochain structure of the phosphorocarbon polymer [53]. The process probably proceeds mainly via a polyaddition reaction.

The reduction of aryldiazonium salts by hypophosphorous acid to aromatic hydrocarbons takes place via a radical-chain mechanism [54]. In the chain initiation stage the hydrogen in the P–H bond adds to the aryl residue [55]; the resulting $H_2\dot{P}O_2$ radicals are probably of the phosphonyl type. Gragerov and coworkers [56] established that the initiation process is of second order with respect to the acid; during the process, chemical polarisation of phenyl protons is observed, probably in the singlet radical pairs $\overline{PhN_2 \cdot H_2PO_2}$.

In contrast to phosphinyl radicals, phosphonyl radicals do not abstract a hydrogen atom from an aromatic ring but add to it. Thus the $(EtO)_2\dot{P}O$ radicals, generated on heating diethyl phosphonate with di-t-butyl peroxide, add to the *para*-position of methyl benzoate with a yield of 65% [5], to the 9-position of anthracene and phenanthrene, to naphthalene and carbazole with formation of a mixture of isomers, and to dibenzofuran [57]. There is no reaction with pyridine and ferrocene.

Arbuzov and Kataeva [58] demonstrated by ESR the formation of triphenylmethyl radicals in the reaction of bromotriphenylmethane with $NaOP(OEt)_2$. Triarylchloromethanes also give rise to free radicals in this reaction [59]. Evidently phosphonyl radicals are formed together with these species, but cannot be detected owing to their rapid recombination.

Levin and coworkers [45,47] investigated the recombination reaction of phosphonyl radicals by the method based on the chemical polarisation of ^{31}P nuclei. The recombination products are the subphosphates $(RO)_2POP(O)(OR)_2$ and the hypophosphates $(RO)_2\overset{\overset{O}{\|}}{P} - \overset{\overset{O}{\|}}{P}(OR)_2$; chemical polarisation of ^{31}P nuclei is observed in both and the multiplet effect (E/A) was noted for tetracoordinate phosphorus. Consequently phosphonyl radicals are ambident: they can recombine both via phosphorus and via oxygen. This conclusion has been confirmed by the isomerisation of hypophosphates to subphosphates at 180°C. [60] Phosphonyl radicals recombine in singlet radical pairs.

The interaction of fluorenylidenetriphenylphosphorane with sodium results in the elimination of phenylsodium and the formation of a radical (I); the reaction of triphenylphosphazophenyl with sodium probably gives rise to the radical $Ph_2\dot{P}{=}NPh$ via the same mechanism [61]. Both radicals are formal analogues of phosphinyl radicals with a P=C or P=N bond instead of P=O.

IV. PHOSPHORANYL RADICALS

1. Generation

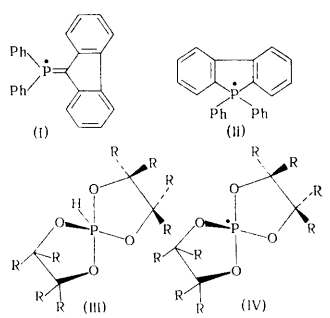
There exist three main methods for the generation of phosphoranyl radicals: the dissociation of the P–X bond in compounds of pentacovalent phosphorus; the one-electron reduction of phosphonium salts, and the addition of radicals to compounds of tervalent phosphorus.

Pentaphenylphosphorane can dissociate into the $\dot{P}Ph_4$ and $\dot{P}h$ radicals [62]. Razuvaev and Osanova [63] established that in chloroform and carbon tetrachloride the reaction products are PPh_4Cl and benzene, while in pyridine the product is phenyldiphenylenephosphine. Razuvaev et al.[64] showed with the aid of a deuterium label that the phenyl group is displaced from the axial and equatorial positions of the PPh_5 molecule with equal ease. In a study of the decomposition of $Ph_4P^{14}C_6H_5$ and $Ph_4PC_6D_5$ in benzene and of pentaphenylphosphorane in hexadeuteriobenzene the same workers [65] established that $\dot{P}Ph_4$ is formed preferentially "in the cage": the fraction of free radicals released into space is 5–6%. The rate of their release, determined [66] by fixation with diphenylpicrylhydrazyl and diphenylpicrylhydrazine, is 2.4×10^{12} species s^{-1} ml^{-1}.

The homolytic dissociation of the P–F bond is not characteristic of phosphorus pentafluoride and its derivatives. The reports [67,68] of the generation of $\dot{P}F_4$ on γ-irradiation of NH_4PF_6 crystals or KPF_6 powders are erroneous (see Section VII). The formation of the $\dot{P}Cl_4$ radical on dissociation of a P–Cl bond in the PCl_5 molecule has not been observed directly, but the reactions of PCl_5 with olefins and alkanes [69] proceed via this stage; the phosphorane $Cl_4PCH_2CH_2R$ is the product in the first case, while PCl_3, HCl, and an alkyl choride are produced in the second.

Bis-(2,2′-biphenylene)phosphorane decomposes in benzene at room temperature with formation of the phosphoranyl radical (II) [70], in which the unpaired electron is apparently delocalised over the π-electron system (a_P = 17.9 G). When spirophosphoranes (III) are acted upon by t-butoxy-radicals, the spirophosphoranyl radicals (IV) are formed [71,72] (see Scheme A).

Scheme A



Cathodic reduction of phosphonium salts leads to the formation of phosphoranyl radicals, which decompose with elimination of one of the ligands and retention of the configuration [73]. The rate of elimination of the ligand decreases in the sequence diphenylmethyl > benzyl > cinnamyl > hydroxymethyl > allyl > β-hydroxyethyl > t-butyl > isopropyl > n-butyl > ethyl > phenyl > methyl. The one-electron mechanism of the reduction of phosphonium salts with formation of phosphoranyl radicals has been confirmed by a polarographic method [74].

Nesmeyanov and coworkers [75] established that the one-electron reduction of tetraphenylphosphonium bromide to the $\dot{P}Ph_4$ radical can occur when the bromide is treated with lithium alkyls; the formation of radicals was confirmed by ESR. The subsequent reaction of the $\dot{P}Ph_4$ radicals depends on the type of electron-donating ion; the reaction products may be triphenylphosphine, phenyldiphenylenephosphine, or even triphenylphosphazophenyl (in the reaction with lithium n-butylamide).

The formation of phosphoranyl radicals from phosphorus(III) compounds was postulated as early as the 1950s by Kamai and Kharrasova [76] for the reaction of mixed alkyl phosphites with carbon tetrachloride, by Ramirez and McKalvie [77] for the reaction of triphenylphosphine with bromoform on ultraviolet irradiation, and by Walling and coworkers [78–80] for the reactions of phosphites and tertiary phosphines with the RO· or RS· radicals. The last two types of reactions have been reviewed [81]. Walling and Rabinowitz [79] proposed the following mechanism for the reaction of trialkyl phosphites with di-t-butyl peroxide:

$$t\text{-}Bu_2O_2 \rightarrow 2\dot{O}Bu\text{-}t \quad , \tag{8a}$$

$$(RO)_3P + \dot{O}Bu\text{-}t \rightarrow (RO)_3\dot{P}OBu\text{-}t \quad , \tag{8b}$$

$$(RO)_3\dot{P}OBu\text{-}t \rightarrow (RO)_3PO + t\text{-}Bu^{\cdot} \quad . \tag{8c}$$

Stage (8c) has been called β-decomposition. Triphenylphosphine interacts with t-butoxy-radicals via the same mechanism [80]. However, in the reaction of tributylphosphine with di-t-butyl peroxide 80% of the reaction product consists of dibutyl t-butylphosphinate and only 20% of tributylphosphine oxide [82]. Thus another pathway is possible in the transformation of phosphoranyl radicals – α-decomposition:

$$R_3\dot{P}OBu\text{-}t \rightarrow R_2POBu\text{-}t + R^{\cdot} \quad . \tag{9}$$

The formation of discrete phosphoranyl radicals via mechanism (8b) was confirmed by different methods. Bentrude and Wielesek [83] showed using a ^{14}C label that this process is irreversible and in addition stereospecific [84]. Levin and coworkers [45,85,86] observed negative chemical polarisation of the ^{31}P nuclei of tributyl and triphenyl phosphates in the reactions of the corresponding phosphites with t-butoxy-radicals, which demonstrated unambiguously the formation of phosphates from singlet radical pairs incorporating phosphoranyl radicals. Negative chemical polarisation of the ^{31}P nuclei of both possible decomposition products of phosphoranyl radicals—$CCl_3P(O)(OEt)_2$ and $BrP(O)(OEt)_2$—and also of triethyl phosphite, in conformity with the possiblity of α-decomposition, has been observed in the photolysis of the triethyl phosphite–bromotrichloromethane system [86].

Finally, phosphoranyl radicals obtained from phosphorus(III) compounds have been detected directly by ESR. Following the irradiation of PF_3, PCl_3, $MePCl_2$, Me_2PCl, and PH_3 in solid matrices, the ESR spectra of $\dot{P}F_4$ [9,10], $\dot{P}Cl_4$ [13], Me_nPCl_{4-n} (n = 1 or 2) [13], and $\dot{P}H_4$ [87] in solid matrices were observed. Kochi and Krusic [89–91] identified phosphoranyl radicals by ESR in the low-temperature photolysis of t-butyl peroxide in the presence of phosphine and mono-, di- and tri-methylphosphines and established that they are rapidly converted into secondary radicals containing two t-butoxy-groups and stable in the course of several minutes.

The stability of primary phosphoranyl radicals is appreciably influenced by the extent to which the phosphorus atom is sterically hindered. For example, the reaction of t-butoxy-radicals with trimethylphosphine results in the formation of the phosphoranyl and methyl radicals (α-decomposition), while only the ethyl radical is formed in the reaction with triethylphosphine [22,91].

Davies et al. [92-94] recorded the ESR spectra of a large number of radicals obtained from trialkyl phosphites via mechanism (8a)–(8b). The formation of phosphoranyl radicals has been confirmed by ESR in the reaction of t-butoxy-radicals with PEt_3, Et_2POEt, and $EtP(OEt)_2$, [95] with *NN*-dimethylamides of phosphorus(III) acids [96,97], and with chlorophosphines and phosphorochloridites [98]. According to the results of Davies et al. [93], methyl and n-butyl radicals do not react with trialkyl phosphites; the ESR spectra of the radicals $(RO)_2(R'O)\dot{P}Me$ were observed in a study [94] of the decomposition of azomethane in the presence of alkyl phosphites at −70°C, but their formation is probably reversible.

Table 4. Parameters of the ESR spectra of $\dot{P}X_4$, $\dot{P}X_3OR$, and $\dot{P}X_2(OR)_2$ radicals.

Radical	g-Factor	Isotropic splitting constants, G			Refs.
		a_P	a_{X_a}	a_{X_e}	
$\dot{P}F_4$	2.0033	1330	282	59 (2F)	9
		1391	360	⩽45 (2F)	10
$\dot{P}O_2F_2$	2.0100	93.8	52.5	—	88
$\dot{P}O_2Cl_2$	2.017	44	4.5	—	41
$\dot{P}H_4$	2.002	973.8	21	21	87
$\dot{P}Cl_4$	2.013	1214	62	7 (2Cl)	13
$MeP\dot{C}l_3$	2.000	1077			13
$(t\text{-BuO})Et\dot{P}OCl_2$	2.011	1145	34.1		98
$(t\text{-BuO})Me\dot{P}Cl_2$	2.010	1023	30.9		98
$(t\text{-BuO})Et\dot{P}Cl_2$	2.010	1003	31.3		98
$(t\text{-BuO})Et_2\dot{P}Cl$	2.008	794	38.9		98
$Me_3\dot{P}OH$	2.009	611.3			40
$(t\text{-BuO})\dot{P}H_3$		626.7	139.6	10.8 (2H)	91
$(t\text{-BuO})\dot{P}H_2Me$		631.5	139.6	9.76 (H)	91
				4.05 (3H)	
$(t\text{-BuO})\dot{P}HMe_2$		631.4	142.6	3.45 (6H)	91
$(t\text{-BuO})\dot{P}Me_3$		618.7	4.6	2.8 (6H)	91
$(t\text{-BuO})_2\dot{P}H_2$		672.5	—	0.6	91
$(t\text{-BuO})_2\dot{P}HMe$		703.3	—	6.84 (H)	91
				3.15 (3H)	
$(t\text{-BuO}_2\dot{P}Me_2$		713.7*		2.5 (6H)	91
		712.4**		2.3 (4H)	91
$(t\text{-BuO})_2\dot{P}Et_2$		713.9		2.3 (4H)	91
		705		2.3 (4H)	95
$i\text{-Pr}_2\dot{P}(OBu\text{-}t)_2$		714.6		1.7 (2H)	91
$Et_2\dot{P}(OBu\text{-}t)_2$		707		2.3 (4H)	95

*From Me_2Ph.
**From Me_3P.

2. Structure

The parameters of the ESR spectra of phosphoranyl radicals are listed in Tables 4 and 5. The hyperfine splittings by the two pairs of ^{19}F nuclei are different in the ESR spectra of $\dot{P}F_4$. [9,10] Consequently $\dot{P}F_4$ must be a structural analogue of the phosphorane PF_4H [99] and must have the structure of a trigonal bipyramid with two fluorine atoms in the axial positions and two in the equatorial positions; the *s* orbital of phosphorus contributes appreciably to the unpaired electron orbital, like the σ orbital of the P–H bond in phosphorane. This model has been confirmed by the observed [100] linear correlation between the a_P constants for $\dot{P}F_4$ and spirophosphoranyl and phosphonyl radicals on the one hand and the spin–spin interaction constants $^1J_{PH}$ for the NMR spectra of the corresponding phosphoranes on the other:

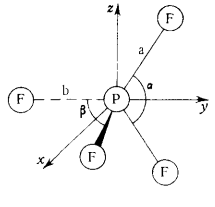
$$a_P = 1.52\,{}^1J_{PH} - 350\ .$$

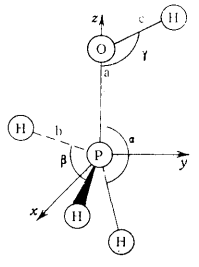
Table 5. Parameters of the ESR spectra of $(R'O)_2(R''O)\dot{P}R$ radicals [94,98].

R	R′	R″	Solvent	g-Factor	a_P, G
Me	Me	Me	Cyclopentane	2.003	783.1
			Hexane	2.003	784.3
Me	Et	Et	Cyclopentane	2.004	786.7
Me	i-Pr	i-Pr	Cyclopentane	2.004	787.4
Me	n-Bu	n-Bu	Cyclopentane	2.004	789.2
Me	t-Bu	t-Bu	Hexane	2.004	884.0
Me	Neopentyl	Neopentyl	Hexane	2.003	803.1
Me	cyclo-C_5H_9	cyclo-C_5H_9	Hexane	2.004	795.8
Me	Me	cyclo-C_5H_9	Hexane	2.003	785.3
Me	Et	cyclo-C_5H_9	Hexane	2.003	789.9
Me	Et	Benzyl	Hexane	2.003	791.2
Cl	Et	t-Bu	Cyclopentane	2.009	1037
Cl	$(CH_2)_2$	t-Bu	Cyclopropane	2.010	1034
Cl	$(CH_2)_3$	t-Bu	Cyclopropane	2.010	1033

Higuchi [101] carried out a quantum-chemical calculation on $\dot{P}F_4$ by the valence bond method and the molecular orbital method in Hoffmann's approximation: comparison of the structural parameters and the calculated spin densities shows that the valence angles in $\dot{P}F_4$ are virtually identical with those in PF_4H. The interatomic distances and the valence angles of $\dot{P}F_4$ have been optimised [23,102] within the framework of the unrestricted Hartree–Fock method (the CNDO/2 approximation) and it has been established that the trigonal bipyramidal structure of $\dot{P}F_4$ is somewhat distorted (Scheme B, Table 6) owing to the marked repulsion of the charges of the fluorine atoms.

Scheme B



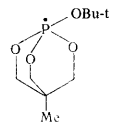


Calculation shows that the unpaired electron orbital of $\dot{P}F_4$ consists largely of the *s* orbital of phosphorus and the p_Z orbitals of the axial fluorine atoms; the d_{Z^2} orbital

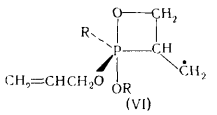
of phosphorus makes a contribution. The calculated *s*-orbital spin density of the phosphorus atom is therefore very large and agrees well with experiment[9,10]. However, the difference between the *s* spin densities at the axial and equatorial fluorine atoms is found to be much lower than follows from ESR data[9,10]; the total spin projection does not eliminate this discrepancy[102]. The higher constants for the splitting by the axial ^{19}F can probably be accounted for by the spin polarisation owing to the high spin density at the $2p_z$ orbitals.

The ESR spectra of $H_3\dot{P}OBu\text{-}t$, $Me\dot{P}H_2OBu\text{-}t$, and $Me_3\dot{P}OBu\text{-}t$ also showed that the ligands are non-equivalent[91], so that these radicals too must have the structure of a trigonal bipyramid close to that of the corresponding phosphoranes. The t-butoxy-group must occupy an axial position and the methyl group in $Me\dot{P}H_2OBu\text{-}t$ must be in an equatorial position according to the Muetterties rule[103]. The hyperfine splitting constant a_P for these radicals is smaller by a factor of two than for $\dot{P}F_4$, which indicates a decrease of the amount of *s* character of the unpaired electron orbital. This phenomenon was initially attributed to the distortion of the trigonal bipyramidal structure of the radicals owing to the decrease of the electronegativity of the ligands[92-94]. However, even a not unduly rigorous calculation on $H_3\dot{P}OMe$ by the CNDO/2 method[104] leads to the conclusion that the equilibrium structure of this radical is very close to that of a trigonal bipyramid. A recent calculation[102] of the optimal geometrical structures of the radicals $\dot{P}H_3OH$ and $\dot{P}H_2(OH)_2$ by the unrestricted Hartree–Fock method in terms of the CNDO/2 approximation showed that this conclusion[92-94] is erroneous: in both radicals the angle between the axial ligands is close to 180° (see Table 6). The calculated spin densities at the axial and equatorial hydrogen atoms in $\dot{P}H_3OH$ are very different, in contrast to the calculation on $\dot{P}F_4$; the use of spin projection yields values very close to the experimental results for $PH_3OBu\text{-}t$.

Scheme C



(V)



(VI)

R = t-BuO, EtO, or Me

R′=CH_2=$CHCH_2$.

According to a calculation[87], the $\dot{P}H_4$ structure is also close to that of an undistorted trigonal bipyramid; the equivalence of the hydrogen atoms observed in the ESR spectrum of $\dot{P}H_4$ has been explained by the fact that the energy barrier to the transition to the configuration with C_{3v} symmetry is very low—about 6 kcal mole^{-1}.

In the light of these data the hypothesis of a tetrahedral structure of the $\dot{P}Ph_4$ radical put forward by Razuvaev et al.[64] will be valid only subject to the condition that the interaction of the phosphorus atom with the benzene rings can alter significantly the geometrical structure of the phosphoranyl radical. This possibility has not been ruled out; Buck and coworkers[105] observed that a_P = 9.7 G (lower by two orders of magnitude than the usual value, see Tables 4 and 5) for the ESR spectrum of the $Ph\dot{P}(OMe)_2OBu\text{-}t$ radical obtained in the low-temperature interaction of dimethyl phenylphosphonate with t-butoxy-radicals and explained this finding by the transition of the radical to a tetrahedral configuration with almost the entire spin density concentrated in the benzene ring. Davies et al.[106] confirmed this result in a study of the ESR spectrum of the $C_6D_5\dot{P}(OMe)_2OBu\text{-}t$ radical; the a_P constants for the $Ph_2POEtOBu\text{-}t$ and $Ph_3POBu\text{-}t$ radicals are also reduced (23.0 and 45.0 G respectively). However, for very electronegative substituents at the phosphorus atoms, the constant a_P for phenylphosphoranyl radicals increases to a value characteristic of the trigonal bipyramidal configuration: for example, a_P = 1009 G for the ESR spectrum of $PhPCl_2OBu\text{-}t$. This spectrum shows a splitting due to the two equivalent ^{35}Cl (and ^{37}Cl) nuclei, which are evidently in the axial positions.

Table 6. Geometry of phosphoranyl radicals according to quantum-chemical calculations.

Radical	Valence angles, deg			Intraatomic distances, Å			Refs.
	α	β	γ	*a*	*b*	*c*	
$\dot{P}H_4$	162	97	—	1.42*	1.42*	—	87
$\dot{P}F_4$	174±5	109±9	—	—	—	—	101
	140	106	—	1.73*	1.73*	—	23
	140.6	105.6	—	1.727	1.722	—	102
$\dot{P}Cl_4$**	180	104	—	1.95	1.95	—	23
$\dot{P}H_3OH$	173.5	98	104.4	1.552 (P—H) 1.730 (P—O)	1.519	1.032	102
$\dot{P}H_2(OH)_2$	174.1	103.1	131.4	1.730	1.532	1.035	102
$\dot{P}H_3O^-$	178.5	95	—	1.565 (P—H) 1.760 (P—O)	1.542	—	102

*Assumed.

**Local minimum; errors in minimisation.

It follows from the ESR data[98] that the chlorine atom in the $(t\text{-}BuO)\dot{P}(OEt)_2Cl$ radical is in the axial position, i.e. is more apicophilic than the alkoxy-groups; this can also be accounted for by the electronegativity factor and by the weaker p_π–d_π P–Cl interaction†.

For the ESR spectra of the $(RO)_4\dot{P}$ radicals, where R is an alkyl substituent, we have g = 2.003–2.004 and a_P = 897 ± 11 G [93,94,107]; for the spirophosphoranyl radicals (IV) at −70°C, a_P = 910 G [71,72]. The constant a_P increases with the electronegativity of R also in bicyclic phosphoranyl radicals; thus a_P = 954.4 G for $(CF_3CH_2O)_2$.(EtO)(t-BuO)$\dot{P}$ [94] and 973.2 G for the radical (V) [93]. The constants a_P for the $(R'O)_2(R''O)R\dot{P}$ radicals, where R′ and R″ are alkyl groups, are also very close (Table 5); the $(t\text{-}BuO)_3\dot{P}Me$ radical is an exception, but these results are probably inaccurate. With decrease of the electronegativity of the ligands, a_P falls and proves to be

†The hydrogen atom in the $\dot{P}H(OMe)_3$ and $\dot{P}H(OH)(OMe)_2$ radicals is in the axial position[213,214], which is consistent with the Muetterties rules[103] when account is taken of the marked apicophilic properties of H.

anomolously high only for $\dot{P}H_4$. It has therefore been suggested that McDowell et al. [87] did not obtain the $\dot{P}H_4$ radicals but some other paramagnetic species [40,98].

3. Reactions of Phosphoranyl Radicals

It is evident from the literature data [80,82] that phosphoranyl radicals are capable of two types of reactions—β-decomposition via mechanism (8c) and α-decomposition, for example:

$$R_3\dot{P}OBu\text{-}t \rightarrow R_2POBu\text{-}t + R^{\cdot} . \qquad (9)$$

These two pathways in the transformations of phosphoranyl radicals can be traced also in the study of Davies et al. [94] The primary radical, for example H_3POBu-t, decomposes via mechanism (9), after which a secondary radical is formed:

$$H_2POBu\text{-}t + \dot{O}Bu\text{-}t \rightarrow H_3\dot{P}(OBu\text{-}t)_2 . \qquad (10)$$

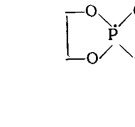
With increase of temperature, this radical probably decomposes via the β-mechanism:

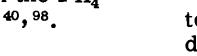
$$H_2\dot{P}(OBu\text{-}t)_2 \rightarrow t\text{-}BuOP(O)H_2 + Bu\text{-}t . \qquad (11)$$

In the presence of an excess of t-butoxy-radicals the reaction can proceed further with formation of the t-BuOP.(O)R and $\dot{P}(BuO\text{-}t)_2$ radicals; one of them has been detected by ESR. [22]

Kinetic studies on the formation of phosphoranyl radicals via mechanism (8b) showed that this reaction is 500–1000 times faster than the abstraction of a hydrogen atom from solvent molecules [5]. The method of competitive reactions has been combined [92-94] with the recording of ESR spectra, which made it possible to determine the rate constants for the overall process $t\text{-}Bu\dot{O} + P(OR)_3 \rightarrow OP(OP)_3 + t\text{-}Bu$ and the β-decomposition of the phosphoranyl radicals [mechanism (8c)] and also the activation energies for these reactions. The kinetic parameters obtained are listed in Table 7. In agreement with the data of Bentrude and Wielesek [83], stage (8b) is irreversible and determines the rate of the entire reaction between the phosphite and the dialkyl peroxide, since the decomposition reaction (10) is slower than the β-decomposition and cannot compete with the latter [94]. The decomposition reaction of PR_3OBu-t and $\dot{P}R_2OBu\text{-}t)_2$ is of first order at 0°C and bimolecular at temperatures between −50° and −60°C. [21,98]

Table 7. Kinetic parameters of the β-decomposition of phorphoranyl radicals.

Radical	$k_{(-60^\circ)}$, s^{-1}	lg A	ΔH, kcal mole^{-1}
$(EtO)_4\dot{P}$	0.36	12.86	12.95
$(t\text{-}BuO)_4\dot{P}$	510		
$(t\text{-}BuO)\dot{P}(OEt)_3$	257	12.95	10.34
$(t\text{-}BuO)\dot{P}(OCH_2CF_3)$	4.5	8.25	7.4
	43.6		

The phosphoranyl radical in which one of the alkoxy-groups has been replaced by a chlorine atom shows a smaller tendency towards β-decomposition, which is believed to be due to the stabilisation of the ground state and the destabilisation of the transition state [98]. Phosphoranyl radicals in which phosphorus is incorporated in a five-membered ring exhibit an even greater resistance to β-decomposition. For example,  does not split off the t-butyl group at 30°C. The spirophosphoranyl radicals (IV) are stable up to 120°C and their β-decomposition is so slow that there is sufficient time for the radicals to dimerise before this happens [71,72]. Both rings of (IV) are probably rigidly fixed. The unusual stability of the radicals (IV) enables them to add to hex-1-ene at −50°C, like phosphinyl radicals.

Phosphoranyl radicals containing prop-2-enoxy- or but-2-enoxy-groups at the phosphorus atom can cyclise with formation of the radicals (VI) in addition to undergoing β-decomposition [107]. The presence of t-butoxy-groups prevents the formation of the five-membered ring and the radicals derived from tri(pent-3-enyl) phosphite do not cyclise at all. a_P = 180 G and $a_{H_\alpha} = a_{H_\beta}$ = 20 G for the ESR spectra of the radicals (VI).

Davies and coworkers [93,94] explained the dual nature of the decomposition of phosphoranyl radicals on the basis of three factors: (1) the stereoselectivity of the decomposition; (2) the comparative stability of the secondary radicals; (3) pseudorotation. It is suggested that, in view of the appreciable weakness of the axial bonds, α-decomposition entails their dissociation while in β-decomposition the equatorial O–C bond is ruptured. It is then evident that the $Me_3\dot{P}OBu$-t radical will decompose via mechanism (10) only, in agreement with the data of Krusic et al. [91] It is also evident that the $R_2\dot{P}(OR)_2$ radical must be much more stable than $\dot{P}(OR)_4$, since the latter can undergo β-decomposition immediately. The $Et\dot{P}(OR)_3$ radical must be more stable than $Et_3\dot{P}OR$, since the dissociation of the P–O bond is more difficult than that of the P–C bond, in agreement with the results of Davies et al. [95]

Furthermore, the rate of β-decomposition is influenced by the nature of the radical removed: the lower its intrinsic stability the greater the difficulty of the β-decomposition and the more stable is the phosphoranyl radical. Consequently the rate constant for the decomposition of $\dot{P}(OBu\text{-}t)_4$ is higher by a factor of 1500 than that for the decomposition of $\dot{P}(OEt)_4$, while the $(PhO)_3\dot{P}OBu$-t radical cannot be detected by ESR at all [93]. In this case steric effects are unimportant, since the rate of decomposition of $\dot{P}(OBu\text{-}t)_4$ is only an order of magnitude higher than that for $t\text{-}BuO\dot{P}(OMe)_3$. [94]

Finally, in order to interpret the decomposition pathway of the phosphoranyl radical, one can employ the concept of pseudorotation proposed by Berry [103]. For example, the t-butoxy-group in the $\dot{P}(OMe)_3OBu$-t radical can enter the equatorial position by pseudorotation and subsequently, by virtue of the comparative stability of the secondary radicals, β-decomposition proceeds via this group [95]. In order to account for the decomposition of the $Et\dot{P}(OEt)_2(OBu\text{-}t)$ and $Et_2\dot{P}(OEt)(OBu\text{-}t)$ radicals with elimination of the ethyl radical [95], the decomposition of the $(t\text{-}BuO)_2\dot{P}(NMe_2)_2$ radical via the α-mechanism, and the characteristics of the reactions of t-butoxy-radicals with phosphoramidites containing five-membered rings, the concept of pseudorotation was also resorted to.

However, it is by no means universal. In the first place pseudorotation in phosphoranyl radicals is frequently inconvenient on energy grounds. Thus the activation energy for the reaction of triethylphosphine with t-butoxy-radicals via the α-mechanism is 1.34 kcal mole^{-1}, that for the α-decomposition of $Et_2\dot{P}(OEt)(OBu\text{-}t)$ is 8.16 kcal mole^{-1} [95], while the energy of pseudorotation in $\dot{P}F_4$ has been estimated theoretically as 25 kcal mole^{-1}, the value for $\dot{P}H_3OH$ being higher still [102]. The broadening of the

components observed in the $\dot{P}H_3OBu$-t ESR spectrum above −70°C [104] is not due to pseudorotation but to the permutation of all the hydrogen atoms. The energy of this process in $\dot{P}H_3OH$ is 1.8–3.4 kcal mole^{-1} [102] and in $\dot{P}H_3OBu$-t the energy is 5.3 kcal mole^{-1} [104]. Even in those cases where pseudorotation in phosphoranyl radicals is possible, it evidently takes place slowly and at best can compete with bond dissociation.

Bentrude and Min [108] obtained evidence for the trigonal bipyramidal structure of phosphoranyl radicals and for the inadequacy of the concept of pseudorotation on the basis of chemical data. They investigated the reactions of phosphites with benzyl radicals via the mechanism

$$PhCH_2\dot{O} + (EtO)_2POR \rightarrow (PhCH_2O)\dot{P}(OR)(OEt)_2 \rightarrow \underset{52\%}{RO(OEt)_2PO} + \underset{44\%}{PhCH_2O(EtO)_2PO} \quad (12a)$$

$$R\dot{O} + (EtO)_2POCH_2Ph \rightarrow (PhCH_2O)\dot{P}(OR)(OEt)_2 \rightarrow \underset{41\%}{RO(OEt)_2PO} + \underset{49\%}{PhCH_2O(EtO)_2PO} \quad (12b)$$

where R = $CH_2C_6H_4Me$-p; the numbers denote the yields of phosphine oxides in reactions (12a) and (12b) respectively. Evidently the alkoxy-groups in the intermediate phosphoranyl radicals are non-equivalent. The new substituent probably enters the axial position, in accordance with the Muetterties rule. If this factor is considered together with the yields of the products, it is found that the β-dissociation in the axial position is 1.3 times faster than in the equatorial position. In this case the pseudorotation factor is unimportant, since pseudorotation is slower than the β-decomposition. The attempt to account for the results [108] by competition between the β-dissociation processes in two axial positions is also invalid, since the introduction of a methyl group in the *para*-position of one of the aryl groups does not affect the ease of β-decomposition.

So far we have considered only the addition of fairly electrophilic radicals to phosphines and their derivatives. On this basis, it has been suggested [109] that a necessary condition for this reaction is a highly polar transition state. However, Davidson [110] established that diphenyl phosphonites react via the β-decomposition mechanism with methyl, isopropyl, and phenyl radicals; the reaction with t-butyl radicals is very slow and that with benzyl radicals does not occur. Fu and Bentrude [111] studied the kinetics of the reaction of trimethyl phosphite with phenyl radicals, which are intermediate between the alkoxy- and alkyl radicals both as regards electrophilic properties and the strength of the P–R bond. The formation of the phosphoranyl radicals $Ph\dot{P}(OMe)_3$ fully predominates in this reaction; next in importance is β-decomposition. The yield of the phosphonate is 99%, i.e. the phosphite absorbs all the kinetically free phenyl radicals. The interaction of methyl radicals with trimethyl phosphate is slower than that of phenyl radicals and triphenylmethyl radicals do not react with the phosphate at all. Fu et al. [112] determined the rate constant k for the molecular interaction of trimethyl phosphite with phenyl radicals ($k = 4.6 \times 10^6$ litre mole^{-1} s^{-1}) and estimated the activation energy for this process as 3.6 kcal mole^{-1}. The addition of phenyl radicals, like that of alkoxy-radicals, is irreversible: $BuOP(OMe)_2$ cannot be obtained from $PhP(OMe)_2$ and $\dot{O}Bu$. Fu et al. [112] suggest that the reaction of $P\dot{h}$ with the phosphite is exothermic; this should be even more true of the reactions of $R\dot{O}$ with phosphites.

Bentrude and coworkers [113–115] examined in detail the energetic aspect of the reactions of phosphorus(III) compounds with alkoxy-radicals. The decisive factor in these reactions is the thermodynamics of the formation of phosphoranyl radicals. The role of polar transition states may be neglected; for example, in the reaction of t-butoxy-radicals with the compounds $XC_6H_4P(OCH_3)_2$, where X = *p*-MeO, H, *p*-Cl, or *m*-CF_3, the polarity of the substituents hardly affects the rate of reaction [$k_{65°} = (3.1 - 3.7) \times 10^8$ litre mole^{-1} s^{-1} for X = H]. The formation of phosphoranyl radicals from the initial products is exothermic and their β-decomposition is more favourable on energy grounds than their α-decomposition owing to the stability of the P–O bond; this probably accounts also for the high reactivity of t-butoxy-radicals with respect to phosphorus(III) compounds. The heat of formation of the radical $\dot{P}X_3Z$ depends on the energy of the rehybridisation of the orbitals, bond energies, and the energy of resonance stabilisation. Thus the preferential occurrence of the α- or β-decomposition of $\dot{P}X_3Z$ is determined by the value of $\bar{D}_{PX_3}$, which is a measure of the P–X bond strength; when $\bar{D}_{PX_3} <$ 75 kcal mole^{-1}, the main reaction product is the phosphite or phosphonite. The formation of α- or β-decomposition products in the reaction with $PhCH_2\dot{O}$ radicals [108] has been explained by the weakening of the C–O bond and the decrease of the free energy of β-decomposition. As was to be expected, the probability of α-decomposition increases in the sequence X = Me < t-Bu < $PhCH_2$. Pseudorotation can be the rate-limiting stage of the process only in the α-decomposition of phosphoranyl radicals. Account must also be taken of the entropy effects.

4. Reactions Involving Phosphoranyl Radicals

Only the mechanisms of the reactions of $\dot{P}Ph_4$ and phosphoranyl radicals formed in the reactions with alkoxy- or phenyl radicals were examined previously. However the range of reactions involving phosphoranyl radicals is much wider. All the reactions involving the autoxidation of phosphines and phosphites have free-radical mechanisms. The oxidation of triethyl phosphite and secondary and tertiary phosphines by nitric oxide [5] and of triethyl phosphite by pyridine *N*-oxide [116], as well as other reactions proceed via the formation of phosphoranyl radicals with subsequent β-decomposition. It is usually believed [5,6] that the radical initiating the oxidation is initially converted into a peroxy-radical, this being followed by the formation of the phosphoranyl radical, whose decomposition initiates the chain:

$$\dot{R} + O_2 \rightarrow RO_2^{\cdot}, \quad (13a)$$

$$PEt_3 + RO_2^{\cdot} \rightarrow Et_3\dot{P}OOR, \quad (13b)$$

$$Et_3\dot{P}OOR \rightarrow Et_3PO + RO^{\cdot}, \quad (13c)$$

$$RO^{\cdot} + Et_3P \rightarrow Et_3\dot{P}OR. \quad (13d)$$

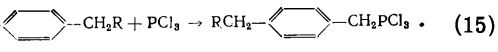
Ultimately $Et_2P(O)OEt$ and $EtP(O)(OEt)_2$ are also formed. Reaction (13b) is bimolecular; $k_{-95°} = 200$ litre mole^{-1} s^{-1} and $\Delta E = 3$ kcal mole^{-1} for PPh_3. [177] However, in these reactions oxygen can add directly to the phosphine or phosphite molecule; this process is possible for triphenyl phosphine and triethyl phosphite, while PCl_3 and $P(OBu\text{-}t)_3$ do not absorb oxygen without an initiator [117]. Phosphoranyl radicals can also combine with O_2; for example $(EtO)_4P\dot{O}O$ radicals ($g = 2.022$ and $a_P = 9.25$ G) and $(t\text{-}BuO)(EtO)_3P\dot{O}O$ radicals ($g = 2.021$ and $a_P = 9.45$ G) were detected [95] at −70°C in the presence of oxygen. Such radicals are stable at −50°C for a few minutes. When the entire oxygen has combined, only the ESR spectrum of the primary phosphoranyl radical is observed [118].

Peroxy-radicals are probably formed also in the oxidation of PCl_3. [4,119]. This reaction is self-initiated with formation of $\dot{P}Cl_2$ and $\dot{C}l$ and then proceeds via the mechanism

$$PCl_3 \xrightarrow{Cl} \dot{P}Cl_4 \xrightarrow{O_2} Cl_4POO\cdot \xrightarrow{PCl_3} 2POCl_3 + Cl\cdot \quad (14)$$

When a hydrocarbon is added to PCl_3 in the presence of O_2, the products are PCl_3 and $PCl_3O\dot{O}$ and ultimately $POCl_3$ and $RPOCl_2$; the compounds $RPCl_2$ were obtained at 575–600°C. [5]

It has already been mentioned (see Section II) that the role of phosphinyl radicals in the reaction of PCl_3 with olefins is insignificant. This reaction proceeds via the formation of the phosphoranyl radicals $Cl_3PCHR'CH_2Cl$ by the addition of $\dot{C}l$ and PCl_3 to the olefin molecule [120]. The reaction of PCl_3 with *p*-xylylene proceeds via the same mechanism; a radical of the benzyl type is formed initially and then reacts with PCl_3 [5]:



The phosphoranyl radical adds to *p*-xylylene as a result of which poly-*p*-xylylene is formed even at −78°C.

The characteristics of the radical reactions of thiols and disulphides with phosphines and phosphites are the same as those of organic peroxides [5,78,112]. The reactivity of phosphorus compounds decreases in this case in the following sequence: $P(n\text{-}Bu)_3 > P(OEt)_3 > PPh_3 > P(OPh)_3$.

Phosphoranyl radicals may also be formed in the reaction of SCl_2, S_2Cl_2, $SOCl_2$, and SO_2Cl_2 with trialkyl phosphites. However, the radical mechanism of these reactions still has to be demonstrated [5].

Apart from the abstraction of a hydrogen atom and an alkyl group and the formation of the radicals discussed in Section V, the reactions of phosphoranyl compounds with phenyl radicals can entail the formation of phosphoranyl radicals by the addition of the phenyl radical to be phosphoranyl oxygen; however, they rapidly disproportionate [121].

V. σ-RADICALS WITH THE PHOSPHORUS ATOM IN THE α- AND β-POSITIONS

When phosphorus acid esters react with hydroxy-radicals in aqueous solutions (for example on treatment with Fenton's reagent), radicals of the type $(R'O)_2P(O)\dot{O}CHR$ or $R'(R'O)P(O)\dot{O}CHR$ (R = H, Me, or Et), which have been detected in a flow system by ESR, are formed [122,123]; the same radicals have been detected in other studies [124], [125] on low-temperature irradiation of trialkyl phosphates. Estimates of Q^H_{CH} for these radicals show that the phosphoryl group has a greater inductive and a weaker mesomeric effect than the acetyl group: a_P = 10–32 G [122,123]; thus the spin population of the 3*s* orbital of phosphorus $\rho_S(^{31}P)$ = 0.003–0.009. The overall spin density at phosphorus in $(R'O)R'P(O)\dot{O}CHR$ radicals is 0.08–0.09; splitting by phosphorus in $(R'O)R''\dot{P}(O)CH_2\dot{C}HR$ radicals has not been observed [123].

β-phosphoryl radicals formed via mechanism (7b) have been detected by ESR [38]. Their $\rho_S(^{31}P)$ is much lower than for phosphonyl radicals (about 0.03); $\rho_S(H)$ for the CH_2 group is of the same order of magnitude—lower than for Et and $(RO)_2P(O)\dot{O}CH_2$. [124] The decrease of spin density at the protons has been explained by the fact that the P–C bond screens the *p* orbital of the unpaired electron and rotation about the C–C bond in the $(RO)_2P\dot{O}CH_2$.$\dot{C}HR'$ radical is hindered.

These results are consistent with the general conclusion of Krusic and Kochi [126] that the conformation with the MR''_3 group displaced from the plane and the maximum overlapping of the electron cloud of the C–M bond and the *p* orbital of the unpaired electron is preferred for radicals of the type $R_2\dot{C}CR'_2MR''_3$ (M is an element in the Third or higher Period). This phenomenon can be explained satisfactorily by the delocalisation of the unpaired electron as a result of hyperconjugation [127]; then the splitting by the ^{31}P nucleus will be proportional to the spin density at the α-carbon atom and $\cos^2\theta$, where θ is the angle between the C–M bond and the axis of the unpaired electron orbital. Damerau et al. [128,129] obtained in aqueous solutions radicals of the type $(RO)_2P(O)CH.$ $.(OR')\dot{C}Cl_2$, which are characterised by a high value of a_P (60–69 G), very sensitive to changes in R and R′, in contrast to a_H; with increase of temperature, a_P decreases sharply in accordance with the hyperconjugation model. The authors [129] estimated θ = 57.2° from the value of a_P. For the radicals $(RO)_2P(O)C\dot{R}'OH$, [128] $a_P \simeq$ 30 G, is independent of temperature, and is probably due to spin polarisation [129].

On the basis of the *g*-factors for the $R_2\dot{C}CR'_2MR''_3$ radicals, Kawamura and Kochi [130] suggested that in these radicals there is a possibility of a direct delocalisation of the unpaired *p* electron over the *d* orbital of M. However, such delocalisation must be insignificant in principle [131]. In the case of phosphorus it does not occur at all, since *g* = 2.0027 for $(MeO)_2P(O)C(OH)Me\dot{C}H_2$ [128], and for $\dot{P}O_3^{2-}$ it is less than 2.002 (see Section VII, 1), while delocalisation over the *d* orbital should lead to a decrease of the *g*-factor.

Low-temperature irradiation of trialkylphosphines yielded radicals of the type $R_2P - \dot{C}R'_2$ [132]; the splitting by the ^{31}P nucleus in their ESR spectra was interpreted as a result of spin polarisation.

Arbuzov et al. [133] investigated the ESR spectra of the phosphonohydrazyl radicals $Ph_2N\dot{N}P(O)R_2$ (R = Ph, OPh, or OEt) in solution. The sum of the constants for the splitting by the two ^{14}N nuclei is lower than for diphenylpicrylhydrazyl; part of the spin density is probably delocalised over the phosphoryl group. A similar result was obtained from the ESR spectra of thiophosphonohydrazyl radicals [134].

VI. RADICAL-CATIONS DERIVED FROM PHOSPHORUS COMPOUNDS

1. Generation

The radical-cations $\dot{P}H_3^+$ [135], $Et_3P^{\dot{+}}$ [135], $Bu_3P^{\dot{+}}$ [135], and $Me_3P^{\dot{+}}$ [136] were obtained by the low-temperature γ-irradiation of phosphine and trialkylphosphines in sulphuric acid at −196°C; irradiation of a mixture of orthophosphoric and sulphuric acids gave $^+\dot{P}(OH)_3$ [137] and not the phosphoranyl radical $\dot{P}(OH)_4$. The dimeric radical-cations $(R_3P)_2^{\dot{+}}$ were detected after irradiation of pure trialkylphosphines [137,138].

Many reactions of phosphines may include a stage involving one-electron oxidation with formation of radical-cations. Ramirez and Dershowitz [139] reported the appearance of ESR signals in the reaction of triphenylphosphine with cloranil. However, these signals were not due to the radical-cations $Ph_2^{\dot{+}}$ but to products of their addition to the oxygen atom in the chloranil molecule [140,141]. The ESR signals in the reaction between triethylphosphite and chloranil have the same origin [141]. ESR signals were also recorded in the triphenylphosphine–sulphur [142], triphenyl-

phosphine–benzoquinone[143], and triphenylphosphine–2,5-dichlorobenzoquinone[144] systems. In the last two cases they are due to semiquinone radicals—derivatives of phosphobetaines; similar stable 4-R-2,6-di-t-butyl-phenoxy-radicals (R = PPh_2, $POPh_2$, $PSPh_2$, etc.) were also investigated[145].

The ESR spectra of the products of the addition of the corresponding radical-cations to 2-methyl-2-nitrosopropane were detected in the reaction of $P(OEt)_3$ and $P(NMe_2)_3$ with 9,10-phenanthrenequinone; in the presence of an excess of $P(NMe_2)_3$, the spectrum of the adduct of the dimeric radical-cation was observed[146].

The anodic oxidation of triphenylphosphine in methanol results in the formation of triphenylphosphine oxide[147], probably via the radical-cation stage. Triarylphosphines can also be converted into the radical-cations $Ar_3P^{\cdot+}$ and then into triarylphosphine oxides under the influence of tetracyanoethylene and tetracyano-*p*-quinodimethane.[148] Dimroth and coworkers[149-151] obtained radical-cations derived from 2,4,6-triphenylphosphabenzene (TPB) and its analogues with two and three C_6D_5 groups by oxidation with phenoxy-radicals, $Pb(OAc)_4$, $Pb(OBz)_4$, or $Hg(OAc)_2$. 1,1-Dimethoxy-, 1,1-diaryloxy-, and 1,1-diaryl-TPB are also readily oxidised to the radical cations[152-154].

Lucken and Mazeline[155] obtained the radical-cation $Ph_3\overset{+}{P}\dot{C}H_2$ by the low-temperature irradiation of triphenylmethylphosphonium chloride; Lyons and coworkers[132,140,156] obtained the radical-cations $R_3'\overset{+}{P}\dot{C}Me$ (R = H, Me, or COPh) in irradiated phosphonium salts‡. After treating aqueous solutions of phosphonium salts with Fenton's reagent, Lucken[157] recorded the ESR spectra of $(HOCH_2)_2\overset{+}{P}\dot{C}HOH$ and $(HOCH_2)_3\overset{+}{P}\dot{C}HOH$.

Buck and coworkers[158,159] generated the radical-cations $Ph_3\overset{+}{P}\dot{C}Ph_2$ and $Ph_3\overset{+}{P}\dot{C}(C_6H_4OMe\text{-}p)_2$ by the anodic oxidation of the corresponding ylides, by the cathodic reduction of the dications obtained by treating the ylides with $AgBF_4$, and by the reaction of the dications with the ylides.

2. Structure

The simplest radical-cation $PH_3^{\cdot+}$ is characterised by an appreciable isotropic interaction of the unpaired electron with the ^{31}P nucleus (Table 8).

According to the theory of the dependence of the valence angles φ in the AB_3 radicals on the nature of the A–B bond[127], the following relation holds between φ and the hybridisation parameter $\lambda = \sqrt{\rho_p/\rho_s}$:

$$\varphi = \arccos\left[\frac{1}{2}\left(\frac{3}{2\lambda^2+3}-1\right)\right] \qquad (16)$$

The use of Eqn. (16) yields $\varphi = 114°$ for $PH_3^{\cdot+}$. Boyd and Whitehead[160] found φ ranging from 112 to 120°, depending on the choice of parameters, when they optimised the $PH_3^{\cdot+}$ geometry by a modified CNDO/2 method. These estimates of φ are probably too high, since the possible involvement of 3*d* orbitals in the formation of bonds was ignored in deriving Eqn. (16) and in the calculations[160]. The inclusion of the 3*d* orbitals of phosphorus in the basis set reduces the total $PH_3^{\cdot+}$ energy and decreases the equilibrium value of φ, as shown by the non-empirical calculation of Aarons et al.[161]; however, the numerical values of φ obtained for $PH_3^{\cdot+}$ in their study are also not entirely reliable owing to the limited basis set employed and the fixed bond length R_{PH}. Gorlov et al.[162] carried out a similar optimisation of the interatomic distances and valence angles in $PH_3^{\cdot+}$ by the UHF – CNDO/2 method; according to their data, $\varphi = 109°27'$ and $R_{PH} = 1.523$ Å, the spin density of the phosphorus *s* orbital being 0.122 after spin projection and the barrier to the $PH_3^{\cdot+}$ inversion being about 15 kcal mole^{-1}. Although these results are not final either, there is no doubt that the $PH_3^{\cdot+}$ radical-cation is non-planar.

Table 8. ESR parameters of radical-cations derived from phosphorus compounds.

Radical	*g*-Factor	Isotropic splitting constants, G		ρ_s (^{31}P)	$\frac{\rho_p}{\rho_s}$ (^{31}P)	References
		$a_{^{31}P}$	a_H			
$PH_3^{\cdot+}$	2.007	517		0.142	6.46	135
$PMe_3^{\cdot+}$	2.016	400		0.110	8.70	136
$PEt_3^{\cdot+}$	2.007	384		0.106	9.29	135,137
$P(n\text{-}Bu)_3^{\cdot+}$	2.008	360		0.099	9.61	135
$P(OH)_3^{\cdot+}$		795		0.218	3.00	40
$(PEt_3)_2^{\cdot+}$		455		0.125	3.31	138
$[P(n\text{-}Bu)_3]_2^{\cdot+}$		462		0.127	3.36	138
$Ph_3\overset{+}{P}\dot{C}H_2$	2.0033	37.0	19.4	0.010		155
$Ph_3\overset{+}{P}\dot{C}MeCOOH$	2.0025	37.0	23.5	0.010		155
$Ph_3\overset{+}{P}\dot{C}Ph_2$		26.6	3.0 (*p*) 2.7 (*o*) 1.2 (*m*)	0.007		158

The valence angles in the radical-cations derived from alkylphosphines, found by Eqn. (16), are greater than for $PH_3^{\cdot+}$, although, according to Walsh's rules for the effect of the ligand electronegativities on the valence angles, their decrease was to be expected; the hyperconjugation of phosphorus with the alkyl groups probably has an effect here[135]. The dimeric radical-cations $(R_3P)_2^{\cdot+}$ have a more pyramidal structure than the monomeric radical-cations. Possibly the radical identified[87] as $\dot{P}H_4$ was in reality the dimeric radical-cation $P_2H_6^{\cdot+}$.

Powell and Hall[148] established that the reactions of optically active arylphosphines with tetracyanoethylene and with tetracyano-*p*-quinodimethane yield the racemic phosphine oxides; consequently the $PH_3P^{\cdot+}$ radical-cation must be planar or must be characterised by a very low inversion barrier. Since the $PH_3^{\cdot+}$ radical-cation is pyramidal, the flattening of the $Ph_3P^{\cdot+}$ structure must be due to the unusual nature of the interaction between the phenyl groups and the phosphorus atom.

A delocalisation of spin density due to the $p_\pi - d_\pi$ interaction is in principle possible in radical-cations where the phosphorus atom can form part of the *p*-electron system. It is observed, for example, in the TPB radical-cation[150-152]. The splitting constants are 22 – 27 G for the ^{31}P nucleus and 2.4 G in each case for the *meta*-protons of the TPB ring and the *ortho*- and *para*-protons of the benzene ring. In the radical-cations derived from 1,1-diaryloxy- and 1,1-diaryl-TPB the unpaired electron is not delocalised over the substituents at the phosphorus atom[152-154]: $a_P = 20$ G.

The rotation of the methylene group in $Ph_3\overset{+}{P}\dot{C}H_2$ is probably hindered[155], also in agreement with the concept of the $p_\pi - d_\pi$ interaction. However, the splitting by the ^{31}P nucleus in the ESR spectra of the radical-cations

‡Irradiation of $Ph_3\overset{+}{P}\bar{C}(Me)COOH$ gives rise to the ESR spectrum of the cyclohexadienyl radical with the phosphorus atom at the methylene carbon atom[215].

$R_3\dot{P}\dot{C}RMe$ [156], $(HOCH_2)_2\dot{P}H\dot{C}HOH$, and $(HOCH_2)_3\dot{P}\dot{C}HOH$ [157] was interpreted as a result of the spin polarisation of the P–C σ bond; the delocalisation of the spin density at the phosphorus atom due to the $p\pi-d\pi$ interaction is very slight according to some investigators [137, 156]. The same conclusion was reached in other studies [158, 159] on the basis of the ESR spectra of $Ph_3\dot{P}\dot{C}Ph_2$ and $Ph_3\dot{P}\dot{C}(C_6H_4.OMe\text{-}p)_2$. The distribution of spin density over the benzene rings and the carbon atom in these radical-cations and in the diphenylmethyl radical [163] is similar; consequently the phosphorus atom is not involved in conjugation and the splitting by its nucleus is due to spin polarisation.

The radical-cations derived from salts of 1,4-diphosphoniacyclohexa-2,5-diene, which are stable at 20°C, have been investigated [164]; $a_P \simeq 16$ G at −60°C and decreases with increase of temperature, possibly in consequence of a change in the conformation of the radical-cation, leading to a change in the hybridisation of the phosphorus atom.

VII. RADICAL-ANIONS DERIVED FROM PHOSPHORUS COMPOUNDS

1. TETRAATOMIC RADICAL-ANIONS

a. Generation

The first phosphorus-containing radical-anion identified by the ESR spectrum was $\dot{P}O_3^{2-}$ in γ-irradiated $Na_2HPO_3.5H_2O$ and $BaHPO_3.6H_2O$ crystals [7]. This radical-anion was also detected after irradiation with X-rays of crystalline magnesium, strontium, and cadmium phosphites [165], ammonium hydrogen phosphate [166], $(NH_4)_2P_2.O_8$ [167], $(NH_4)_2PO_3F.H_2O$ [168], and $CaCO_3$ with an admixture of phosphite [169]; Schlick et al. [170] studied the ESR spectrum of $\dot{P}O_3^{2-}$ in irradiated $Na_2DP^{17}O_3.5D_2O$ crystals. Morton [171] recorded the ESR spectrum of the HPO_2^- radical-anion in a γ-irradiated ammonium hypophosphite single crystal and Atkins et al. [172] obtained this spectrum for irradiated crystals of sodium and magnesium hypophosphites. Fessenden [173] detected by ESR the FPO_2^- radical-ions in NH_4PF_6 and these were subsequently also found [174] on γ-irradiation of KPO_2F_2. The HPO_2^- and $\dot{P}O_3^{2-}$ radical-ions were obtained in aqueous solutions almost simultaneously by Beckwith [175] and by Norman and coworkers [176] by treating hypophosphorous and phosphorous acids with Fenton's reagent; the latter yields the HPO_3^- radical-ion in an acid medium [175]. Low-temperature irradiation of dimethyl and diethyl phosphites gave, apart from phosphonyl radicals, also the $MeOPO_2^-$ and $EtOPO_2^-$ radical-ions, while only the latter radicals were found in frozen solutions of phosphites in 2-methyltetrahydrofuran [37]. Irradiation of solid phenylphosphinic acid salts with X-rays [177] and their treatment with Fenton's reagent in aqueous solutions [176] yielded the $PhPO_2^-$ radical-anion, while the neutral $Ph\dot{P}(O)OH$ radical was obtained in irradiated phenylphosphinic acid powder [177].

b. Structure

The parameters of the ESR spectra of the simplest phosphorus-containing radical-anions are presented in Table 9. Judging from the values of ρ_P/ρ_S, these radical-anions must be non-planar [178], particularly if the contribution of the 3*d* orbitals of phosphorus to the formation of bonds is considerable (see Section VI). The numerical value of the valence angle in $\dot{P}O_3^{2-}$ depends on the nature of the matrix. With increase of the ρ_P/ρ_S ratio, the overall spin density at the phosphorus atom diminishes; in this respect the $\dot{P}O_3^{2-}$ radical-ion differs from NO_3^{2-}. [179]

A quantum-chemical calculation on $\dot{P}O_3^{2-}$ with a pyramidal structure [168] by the molecular orbital method in Hoffmann's approximation led to a satisfactory agreement between the calculated and experimental splitting constants. After optimising the $\dot{P}O_3^{2-}$ geometry by the unrestricted Hartree–Fock method in terms of the CNDO/2 approximation, Kilcast and Thomson [23] found that the energy minimum corresponds to a planar structure ($\varphi = 120°$, $R_{PO} = 1.69$ Å). According to their data [23], the HPO_2^- and FPO_2^- radical-ions are non-planar. All the calculated *s* spin densities are somewhat higher than the experimental values; it was noted that the *s* spin density at the phosphorus atom increases as the radical-ion becomes flattened, contrary to Walsh's rule [127].

Table 9. ESR parameters of phosphorus-containing radical-anions.

Radical	*g*-Factor	Isotropic splitting constants, G		ρ_s (^{31}P)	$\frac{\rho_p}{\rho_s}$ (^{31}P)	Refs.
		$a_{^{31}P}$	a_X			
$\dot{P}O_3^{2-}$	2.0003	594		0.163	3.21	7
	1.999	675		0.185	3.00	165
		627		0.172	3.16	166
	2.0008	751		0.206	2.65	167
		554		0.152	2.72	168
	2.0016	700		0.192	3.01	169
	2.0014	571		0.157		175
	2.0018	644		0.177		176
HPO_3^-	2.0020	658		0.181		175
HPO_2^-		495	82.5 (^{1}H)	0.136		171
	2.0028	484	90	0.133		175
	2.0028	478	89.5	0.131		176
$MeOPO_2^-$		556		0.153	2.94	37
$EtOPO_2^-$		557		0.153	2.99	37
FPO_2^-	2.001	699	169 (^{19}F)	0.192		173
$PhPO_2^-$	2.0001	468		0.129		176
	2.0030	490.5–514		0.135–0.141	4.17–4.35	177
$\dot{P}O_4^{2-}$	2.015	29		0.008		195
$\dot{P}O_4^{4-}$	2.0106	1156		0.318	1.74	196
$POCl_3^-$	2.018	1359	67 (2 ^{35}Cl) 15 (^{35}Cl)	0.373		41
		1371	40 (2 ^{35}Cl) 18 (^{35}Cl)	0.376		201
$(PhPOCl)_2^-$	2.009	1000	51 (2 ^{35}Cl)	0.275	2.67	216
$(PNCl_2)_3^-$		1290		0.354		224

The increase of A_{iso} (^{31}P) and the enhancement of the pyramidal structure of the radical-ion on passing from $\dot{P}O_3^{2-}$ to HPO_3^- has been explained by a decrease of the repulsion between the electronic charges as a result of protonation. However, the qualitative distribution of spin density is not altered either by protonation or by the addition of an alkyl group. The $PhPO_2^-$ radical-anion is undoubtedly non-planar, in contrast to the $PhNO_2^-$ radical-anion. The valence angles in $PhPO_2^-$ are unknown; the *s* spin density at the phosphorus atom increases on protonation of $PhPO_2^-$ and depends on the type of cation in the matrix [177]. As a result of both these effects, the $PhPO_2^-$ radical-anions resemble more closely $\dot{P}O_3^{2-}$ and other tetra-atomic radical-ions.

c. Reactions of XPO_2^- Radical-anions

It follows from the foregoing that the $\dot{P}O_3^{2-}$ and HPO_2^- radical-anions can be regarded as dealkylated phosphonyl radicals. Since the influence of the alkyl groups is relatively slight [37, 38], presumably the chemical properties of

these radical-anions will resemble those of phosphonyl radicals. Indeed they are capable of reducing alkyl bromides, alkyl iodides, bromo- and iodo-substituted carboxylic acids, and diacetyl to alkyl radicals and phenyldiazonium salts to phenyl radicals ($\dot{P}O_3^{2-}$ is the most effective reducing agent[175]) and can also add to the C=C double bond in maleic, acrylic, and methacrylic acids and their anions, and 1,1-dimethylethylene and to the C=N bonds in $CH_2{=}NO_2^-$ and oximes[175,176]. However, the addition proceeds with greater difficulty than that of the $\dot{O}H$ and $\dot{N}H_2$ radicals and only to a carbon atom not bound to a polar group. It follows from the analysis of the ESR spectra of the radical addition products that the spin density is delocalised over the phosphorus atom; free rotation about the P–C bond is hindered; according to Beckwith[175], this can be explained only by the interaction of the unpaired electron with the 3*d* orbitals of phosphorus. The reactions of $PhPO_2^-$ in solution are similar to those $\dot{P}O_3^{2-}$ and HPO_2^-.

When irradiated NaH_2PO_3 is dissolved in aqueous solution of t-butyl nitroxide, $\dot{P}O_3^{2-}$ adds to the nitrogen atom of the N=O bond [175]. A similar reaction takes place between nitrobenzene or *p*-nitrobenzoic acid and $\dot{P}O_3^{2-}$ or HPO_2^-. [176]

2. RADICAL-ANIONS DERIVED FROM PHOSPHINES

The unpaired electron in the radical-anion derived from a phosphorus(III) compound can be stabilised by delocalisation of the π-electron system and can occupy the lowest vacant π orbital. In this case the nature and degree of its delocalisation are related to the degree of involvement of phosphorus in the π-electron interaction.

Arylphosphines are reduced over alkali metals at temperatures between −40° and −80°C to the corresponding radical-anions. However, when this method is used, one has to bear in mind the possibility of their conversion into more stable secondary paramagnetic products. Thus, on reducing triphenylphosphine over potassium, Hanna[180] obtained the phosphyls Ph_2PK, which are also formed when triphenylphosphine reacts with lithium and sodium[181], and not the PPh_3^- radical-ions; as a result, his data[180] concerning the structure of PPh_3^- are erroneous. In the ESR spectra of phosphides a_P = 8.0–8.4 G, regardless of the choice of alkali metals; splitting by the protons in the benzene rings is also observed[181]. The true radical-anions derived from triphenylphosphine, methyldiphenylphosphine, and dimethylphenylphosphine were apparently investigated by Kabachnik and coworkers[182,183], who concluded that the spin density is delocalised over several benzene rings. On reduction of dimethylphenylphosphine over potassium at −90°C, Eliseeva et al. [184] obtained an ESR spectrum with splitting by the ^{31}P nucleus and the benzene ring protons. According to these workers[184], the distribution of spin density corresponds to the vacant orbital of benzene stabilised by an electron-accepting substituent. Gerson et al. [185] showed that the Me_2PPh^- radical-ion is stable over sodium at −40°C and confirmed the electron-accepting properties of the dimethylphosphino-group, although their hyperfine splitting constants differ from those quoted by Eliseeva et al. [184], in particular $a_{H(para)}$ = 8.9 G and a_P = 7.2 G. Since the inductive effect of the dimethylphosphino-group should be positive (electron donating), its electron-accepting properties can be accounted for only by an additional interaction of the π electrons of the benzene ring with 3*d* orbitals of phosphorus. The Me_2PPh^- radical-ion is unstable over potassium[185] and is converted into a secondary radical whose ESR spectrum has been published[184] with an erroneous assignment of the splitting constants; the nature of the secondary radical is not clear. Hnoosh and Zingaro[186] established that the radical-anion derived from tris-(α-naphthyl)phosphine is readily converted in the range between 0° and −65°C into naphthalene radical-anions over sodium and into the phosphyls $(C_{10}H_7)_2PK$ over potassium.

A more reliable method of generating phosphine radical-anions is electrochemical reduction, which can be carried out strictly at the reversible electron transfer stage. The formation of the Me_2PPh^- radical-anion was confirmed by this method in combination with ESR spectra[185]. Triphenylphosphine is also reduced at the cathode to a radical-anion[187–189]; the electrochemical reduction of Ph_2PCl and $PhPCl_2$ immediately leads to the elimination of the Cl^- ion, by-passing the radical-anion stage[187]. According to Santhanam and Bard[188] the Ph_3P^- radical-anion is unstable, readily splits off Ph^-, and is then converted into diphenylphosphine. However, when the reduction potential is controlled within the limits corresponding to the one-electron stage, the Ph_3P^- radical-anions can be generated in amounts sufficient for their detection by ESR [189]. Il'yasov et al. [190] refined the proton splitting constants for the Ph_3P^- radical-anion by deuteriating the phenyl groups and confirmed that the unpaired electron is delocalised over all three benzene rings (for further details, see Section VII, 3).

The electrochemical reduction of the phosphines $p\text{-}XC_6H_4P(C{\equiv}CC_6H_4NO_2\text{-}p)_2$ (X = H, Cl, or NMe_2) in tetrahydrofuran or dimethoxyethane[191] results in the formation of radical-ions where the unpaired electron is localised in the fragment $>PC{\equiv}CC_6H_4NO_2\text{-}p$ (a_N = 7.4–7.8 G; a_P = 0.9–1.3 G). The polarogram of the phosphine resembles that of nitrobenzene in a non-aqueous medium. The presence of powerful electron-accepting groups probably prevents the delocalisation of the unpaired electron. The competitive effect of the electron-accepting group is manifested also in the ESR spectra of ethyl benzoates containing the R_2P group in the *para*- or *meta*-positions[192]. For *para*-substituted radical-anions, a_P = 3.8–5.2 G, which is appreciably lower than a_P for the radical-anion derived from dimethylphenylphosphine[185]; for *meta*-substituted radical-anions, a_P = 1.1–1.3 G and the distribution of spin density in the benzene ring changes little compared with the unsubstituted ethyl benzoate.

3. RADICAL-ANIONS DERIVED FROM PHOSPHORINS AND PHOSPHOLES

The ESR spectrum of the radical-anion derived from TPB shows splitting only due to the ^{31}P nucleus (a_P = 32.4 G) or, in other words, the lowest vacant orbital of TPB is more localised at the phosphorus atom than the highest occupied orbital[150,151,193]. A similar phenomenon has been observed also in the ESR spectra of the radical-anions derived from 1,1-dimethoxy- and 1,1-diphenoxy-TPB (a_P = 31.6 G) [152]. For the ESR spectrum of the TPB radical-trianion, a_P = 4.6 G. [151] Märkl and Merz[154] reported radical-anions derived from 1,1-diaryl-TPB.

Thomson and Kilcast[194] obtained the radical-anions derived from 1-R-2,5-diphenylphospholes: a_P = 23.5 G for R = Me and a_P = 26.5 G for R = Ph. On the basis of these results, and Dimroth's ESR data[152–154] for the phosphorin radical-anions and radical-cations, Thomson and Kilcast[194] attempted to estimate the constant Q^P_{eff} for the σ–π polarisation at the phosphorus atom. The spin density

$\rho\pi(P)$ was calculated by the McLachlan method. Q^P_{eff} = 97.9 G was found from the aP for the phosphorin radical-cations, which is close to the values of Q^P_{eff} obtained from aP for $\dot{P}H_2$, $\dot{P}F_2$, AND $\dot{P}Cl_2$ and from calculations on these radicals by the CNDO/2 method[23]. The values of Q^P_{eff} obtained from the aP for the radical-anions derived from phosphorins and phospholes are 31.7 and 725.4 G respectively. The ^{31}P σ–π interaction constants probably depend strongly on the charge at the phosphorus and adjoining atoms. Thomson and Kilcast[194] attempted to take into account the influence of the adjoining atom in the two-parameter equation $a_P = Q^P_{PP}\rho(P) + Q^P_{CP}\rho(C)$ and found that Q^P_{PP} = 39 G and Q^P_{CP} = 28.6 G.

4. PENTAATOMIC RADICAL-ANIONS

All the radical-anions of this type which have been studied experimentally were obtained by the low-temperature γ-irradiation of solids. The ESR spectra of the $\dot{P}O_4^{2-}$ radical-ion in irradiated phosphates and pyrophosphates have been studied in a number of investigations[127, 195-197]; aP depends on the environment of the radical, as for $\dot{P}O_3^{2-}$. The hypothesis[127] that $\dot{P}O_3$ and not $\dot{P}O_4^{2-}$ is formed in many cases has been confirmed to some extent by a quantum-chemical calculation[23], although its results require serious revision.

The ESR spectrum of a radical which Symons identified[199] as $\dot{P}O_4^{4-}$ was observed for irradiated phenacite [198]; this identification is probably correct[200]. The value of aP for $\dot{P}O_4^{4-}$ is much higher than for $\dot{P}(OR)_4$ radicals[92-94] (Tables 5 and 9). This result is strange from the standpoint of the general rule concerning the increase of aP for $\dot{P}X_4$ with increasing electronegativity of the ligand X, [13, 40] particularly since aP = 860 G for the $(MeO)_3PO^{\cdot-}$ radical-anion, formed[40] in γ-irradiated phosphate together with $Me_2\dot{P}O$, which is less than the value for $\dot{P}(OMe)_4$. The "$\dot{P}O_4^{4-}$ anomaly" has been explained[40] by the influence of the surrounding Be^{2+} cations; it is suggested that aP < 900 G for $\dot{P}O_4^{4-}$ in weaker fields. In the $PO_3F^{\cdot-}$ radical-anion the unpaired electron is highly localised at the oxygen atom[88].

A quantum-chemical calculation[102] for the hypothetical $PH_3O^{\cdot-}$ radical-anion by the CNDO/2 method showed that its equilibrium geometry is almost the same as that of PH_3OH (Table 6), namely trigonal bypyramidal. This result is consistent with the data of Begum and Symons[41] and also of Gillbro and Williams[201] for the ESR spectrum of $POCl_3^{\cdot-}$ radical-anions; in both cases there is splitting by the two equivalent ^{35}Cl nuclei corresponding to the axial positions and a smaller splitting due to the third (equatorial) ^{35}Cl nucleus. The radical-anions have been generated[41] in polycrystalline $POCl_3$, which led to unduly high constants for isotropic splitting by axial ^{35}Cl. A study[201] of the ESR spectra of the radical-anions in irradiated $POCl_3$ single crystals showed that these constants are consistent with data[98] obtained from the ESR spectra of chlorophosphoranyl radicals in solutions. Consequently the chlorine atom in these radicals is fixed in the axial position and there is no pseudorotation. Furthermore, anisotropic splitting by the axial ^{35}Cl ($B_{||}$ = 30 G), corresponding to a spin density of 0.29 in the $3p\sigma$ chlorine orbital, has been observed[201].

According to calculations[102], the distribution of spin density in the $PH_3O^{\cdot-}$ radical-anion differs significantly from that in the neutral $\dot{P}H_3OH$ radical; in particular the s spin density at the phosphorus atom is reduced by an order of magnitude in the radical-anion.

5. THE RADICAL-ANIONS DERIVED FROM PHOSPHINE OXIDES AND PHOSPHATES

Begum and Symons[43] reported that the $Me_3PO^{\cdot-}$ radical-anion, whose aP is fully consistent with the ESR data for $Me_3POBu\text{-}t$ [91] (splitting by methyl protons was not observed[43]), is formed in γ-irradiated trimethylphosphine oxide. This result is inconsistent with the above data obtained by quantum-chemical calculation[102]. It is therefore more likely that Begum and Symons[43] obtained the ESR spectrum of the $Me\dot{P}OH$ [$Me_3\dot{P}OH$? (Ed. of Translation)] radical.

The radical-anions derived from triphenylphosphine oxide[182,183,202], trialkyl phosphine oxides[182,183,203], and alkylarylphosphine oxides[182,183] are formed when these compounds are reduced over an alkali metal in tetrahydrofuran or dimethoxyethane. Il'yasov and coworkers[189,204] showed that, in the electrochemical reduction of triphenylphosphine oxide, triphenylphosphine sulphide, and diethyl β-styrylphosphinate, the first stage is reversible addition of one electron.

The ESR spectra of the radical-anions of all the above compounds generated by this method have been investigated[189,205]. For an unambiguous assignment of the splitting constants in the ESR spectra, a study was also made[190] of the radical-anions $Ph_2(C_6D_5)PO^{\cdot-}$, $Ph(C_6D_5)_2PO^{\cdot-}$, and $(C_6D_5)_3PO^{\cdot-}$. It was established that, as in the triphenylphosphine radical-anion, the unpaired electron is equally delocalised over all three benzene rings and also over the phosphorus atom (aP = 4 G). Such delocalisation cannot be accounted for within the framework of the π-electron model; the unsatisfactory result of the calculation on $Ph_3PO^{\cdot-}$ by the Hückel method confirmed this. Possibly it is dynamic, as in the radical-anions derived from tetraphenylsilane and diethyldiphenylsilane [206], the main feature of such delocalisation being a marked dependence of the rate of electron transfer from one aromatic fragment to another on the counterion solvation conditions[207]. Cowley and Hnoosh[208] studied the $Ph_2(NMe_2)PO^{\cdot-}$ radical-anions generated by reduction over metallic sodium. It follows from the ESR spectra obtained[208] that the spin density is delocalised over the phosphorus atom and one benzene ring; the splitting constants for the $Ph(NH_2)MePO^{\cdot-}$ radical-anion are aP = 8.75 G, aH(para) = aH(ortho) = 3.5 G, $a_{H(Me)}$ = 0.38 G, and a_N = 4.9 G. The π conjugation of the phosphoryl group with the benzene ring probably occurs more readily than with other substituents. Calculation of the spin densities in terms of the π approximation by the McLachlan method gives rise to a satisfactory agreement with experiment. Kabachnik and coworkers [192] generated the m- and p-$R_2P(O)C_6H_4COOEt$ (R = Me, Et, or i-PrNMe$_2$) radical-anions by electrochemical reduction in acetonitrile at –40°C. The ^{31}P splitting in the ESR spectra of the *para*-substituted radical-anions is fairly large (aP ≃ 13 G), increasing somewhat with increase of the bulk of R; slight splitting due to the R protons has also been observed (a = 0.3–0.6 G). The ESR spectra of *meta*-substituted radical-anions are characterised by the absence of splitting due to ^{31}P and the protons in R; other splitting constants differ little from those for the ethyl benzoate radical-anion. The splitting constants for the protons in the *ortho*-position relative to the ethoxycarbonyl group are correlated with the constants $\sigma_{eff} = \sigma_{R(m)} + 0.23\sigma_I$ of the substituents R_2P, $R_2P(O)$, $R_2P(S)$, and simpler groups.

Allen and Bond[209] studied the radical-anions obtained from semiquinone-phosphates derived from benzo- and

naphtho-quinones. a_P = 1.3 G for the p-$OC_6H_4O\dot{P}O_3^{2-}$ radical-anion; after the introduction of four methyl groups, a_P = 17.2 G. Allen and Bond[209] believe that the hyperconjugation model, in which the spin density is transferred directly from the $2p\pi$ orbital of carbon to the 3s orbital of phosphorus, is most suitable for these radical-anions; spin polarisation is less likely. Gulick and Geske[210] generated radical-anions derived from dialkyl p-nitrophenyl and diaryl p-nitrophenyl phosphates by electrochemical reduction and observed in their ESR spectra splitting due to the protons of the p-nitrophenyl group and the ^{14}N and ^{31}P nuclei. The splitting constant a_P = 7–8 G, increasing to 13.6 G for the $(EtO)_2P(O)CH_2C_6H_4NO_2$-$p^{\cdot-}$ radical-anion. They suggested[210] that the transfer of spin density to phosphorus takes place via a hyperconjugation mechanism, although a_P did not change in the range from +25° to −45°C. Gulick[211] interpreted the splittings by the ^{31}P nucleus in the ESR spectra of the radical-anions derived from O-(diphenylphosphoryl)-2,6-di-R-4-nitrophenols in terms of a compound model combining the spin polarisation and hyperconjugation effects. For the $(PhO)_2$.$P(O)SC_6H_4NO_2$-$p^{\cdot-}$ radical-anion, a_P = 24.8 G, either in consequence of direct π conjugation due to the 3d sulphur orbitals or because the PSC valence angle is smaller than the POC angle, which leads to a greater degree of transfer of spin density to phosphorus via the hyperconjugation mechanism. The values of a_N and the potentials $E_{\frac{1}{2}}$ for the radical-anions which he investigated[211], led Gulick to the conclusion that the electronic effects of the $Ph_2P(O)O$ group and the hydrogen atom are approximately the same.

Lassmann et al.[212] established that the splitting constants a_N and a_P for the ESR spectra of the radical-anions derived from diethyl p-nitrophenyl phosphate (paraoxon) and dimethyl p-nitrophenyl phosphate (parathion) are somewhat different. Furthermore, they depend on the anion of the salt used as the supporting electrolyte: a_P is 6.12 G for the parathion radical-anion with NEt_4I and 9.71 G with NEt_4ClO_4. Evidently the radical-anions generated electrochemically form association complexes with the ions of the supporting electrolytes; the spin densities at the phosphoryl group and other polar groups are sensitive to the nature of these complexes.

The $PhP(O)Cl_2^{\cdot-}$ radical-anion, generated by the γ-irradiation of $PhP(O)Cl_2$ at −196°C[216], has a trigonal bipyramidal structure with appreciable localisation of the unpaired electron at the s orbital of phosphorus, as in $POCl_3^{\cdot-}$ (Table 9). When there are two possible ways of adding an electron to the molecule (to the phosphorus atom or the benzene ring), the preferred mode of addition probably depends on the relative electron affinities of the two centres and at low temperatures also on the degree of distortion necessary for the formation of the most stable conformation of the radical-anion[217]. The three-centre σ^* Cl–P–Cl molecular orbital should therefore lie below the π^* molecular orbital of the benzene ring.

6. RADICAL-ANIONS WITH A P = N BOND

The ESR spectra of the $R_3PNC_6H_4NO_2$-$p^{\cdot-}$ radical-anions derived from phosphazo-compounds and generated at the cathode in acetonitrile or dimethylformamide have been investigated[218–220]; the first stage of the electrochemical reduction of these substances is a reversible one-electron process[221]. The splitting constants are $a_{N(NO_2)}$ = 11.0–13.5 G and a_P = 3.5–5.5 G; both constants depend on the electron density of the substituents R. If one of these is R = Ph, a slight (0.2–0.3 G) splitting by the protons of this benzene ring is also observed. The authors[218–220] concluded that the radical-anions from phosphazoarenes contain a π-electron system incorporating the phosphazo-group. The π-electronic structure of the phosphazoarenes and the spin densities were calculated on this hypothesis by the Hückel and McLachlan methods respectively[222]. The calculated energies of the lowest vacant π orbitals are correlated with the potentials $E_{\frac{1}{2}}$ of the phosphazoarenes[221] and the splitting constants found from the calculated spin densities agree very well with experiment. The splitting by the ^{14}N nucleus of the imino-nitrogen does not exceed 0.2 G according to the calculation[222] and is not therefore observed in the ESR spectra[218,219].

The unpaired electron in the $Ph_3PNXC_6H_4NO_2$-$p^{\cdot-}$ (X = S or SO) radical-anions is delocalised only over the p-nitrophenyl residue[218]. Thus the –S– and –SO– bridging groups prevent the inclusion of the phosphazo-group in the π-conjugation system. This system also breaks down in the $(p\text{-}F_3CC_6H_4)_3POC_6H_4NO_2$-$p$ radical-anion, the ESR spectrum of which resembles that of the p-nitroaniline radical-anion[219]; in this case the 3d orbitals of phosphorus are probably involved preferentially in the formation of the P–R bond and not P–N.

Allcock and Birdsall[223] generated the $(PNR_2)_3^{\cdot-}$ radical-anions where R = Ph or OAr, by an electrochemical method in dimethylformamide; under these conditions, $(PNF_2)_3$ and $(PNCl_2)_3$ are not reduced to the radical-anions. It follows from the ESR spectra of the radical-anions obtained by Allcock and Birdsall[223] that the unpaired electron is not delocalised over the phosphazene ring. This conclusion was fully confirmed by Mishra and Symons[224], who obtained the ESR spectrum of $(PNCl_2)_3^{\cdot-}$ on low-temperature γ-irradiation of the phosphonitrilic chloride trimer. It is characterised by an appreciable isotropic splitting by one of the ^{31}P nuclei. Thus the unpaired electron is localised at one phosphorus atom, whose hybridisation probably corresponds to the configuration of a trigonal bipyramid, as in phosphoranyl radicals.

7. THE $PF_5^{\cdot-}$ RADICAL-ANION

Morton[67] observed the isotropic ESR spectrum of a radical containing a phosphorus atom and four equivalent fluorine atoms on irradiation of NH_4PF_6 at about 20°C[67]; the radical was identified as $\dot{P}F_4$. Atkins and Symons[68] observed a similar spectrum on γ-irradiation of KPF_6 and noted that it becomes appreciably broadened at −63°C; at −73°C and below the fluorine atoms become non-equivalent, which is believed to be a consequence of the "freezing" of the pseudorotation in PF_4. Mishra and Symons showed recently[225] that an additional doublet splitting is observed in this spectrum (a = 2.3 G); consequently the paramagnetic species formed is the radical-anion $PF_5^{\cdot-}$ and not $\dot{P}F_4$. This process is more likely also on general grounds. Four fluorine atoms in $PF_5^{\cdot-}$ remain equivalent also at both 20° and −196°C; the broadening of the components of the ESR spectrum observed by Atkins and Symons[68] can be explained by the hindered rotation of the entire radical-anion and not by pseudorotation.

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On the whole one may conclude that the free radicals and radical-ions derived from phosphorus compounds constitute a fairly specific class of radical species. Only the properties of phosphinyl radicals resemble those of

aminyl radicals to which the former are formally analogous. The properties of other phosphorus-containing free radicals are determined to a large extent by the characteristics of the nature of the chemical bonds involving phosphorus relative to those of the elements in the Second Period. A detailed study of their properties is undoubtedly important for the development of ideas concerning the stereochemistry and reactivity of phosphorus compounds.

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Alkylene Diphosphine Dioxides as Extractants and Complex-forming Agents

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Alkylenediphosphine dioxides are a new group of highly effective complex-forming agents capable of binding metal ions to form chelate rings. The review discusses methods for the synthesis of neutral bidentate organophosphorus complex-forming agents based on diphosphine dioxides, their extraction properties, and the possibility of the modification of the structural and steric factors which influence significantly the complex-forming properties of the ligand.
The bibliography includes 133 references.

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1. INTRODUCTION

One of the characteristic properties of organic compounds of phosphorus is their ability to form complexes with metal ions. The study of these properties of organophosphorus compounds is not only of theoretical interest but also leads to the solution of many important practical problems.

Extensive study of the complex-forming properties of organic derivatives of quinquevalent phosphorus was stimulated by the development of the atomic energy industry which gave rise to a vigorous search for methods whereby complex mixtures of metals could be separated. Compounds containing P=O bonds proved to be highly effective for this purpose. Since then organophosphorus compounds, mainly phosphates, have been widely used in technology as extractants with isolation and concentration of metals.

Further development and improvements in this field have proceeded on lines designed to create more effective complex-forming agents, more selective with respect to individual groups of metal ions, and more universal in their applications. All these problems are now of urgent importance owing to the rapid development of technology and analytical chemistry.

Among the neutral organophosphorus complex-forming agents containing phosphorus(V) which have now been investigated tertiary phosphine oxides exhibit the greatest complex-forming capacity. Their effectiveness greatly exceeds that of phosphates, phosphonates and phosphinates. Although the ability of phosphine oxides to form complexes varies as a function of their structure and the nature of the substituents at the phosphorus atom, the variation do not exceed significantly an order of magnitude.

Fundamentally different possibilities of improving the effectiveness and selectivity of the complex-forming phosphine oxides arise when the chelate-forming effect is used. For this purpose, it is necessary to have substances containing in the molecule at least two and possibly more phosphine oxide groups, when the complex-forming capacity can be enhanced as a result of the formation of rings with the metal ions involving two or several phosphoryl groups.

One of the new trends in the field of organophosphorus complex-forming agents in fact constitutes the synthesis of substances with the structure of polydentate ligands. This group of substances is of interest also because it gives rise to extensive possibilities for the modification of the structural and steric factors which influence significantly the complex-forming properties of the ligands.

In 1968 Kabachnik et al.[1] published a review on the methods of synthesising organophosphorus complexones and their complex-forming properties. This paper is devoted to neutral bidentate organophosphorus complex-forming agents based on alkylenediphosphine dioxides† and consists of two parts: the first discusses the method of synthesising compounds of this class and the second deals with data on their extraction and complex-forming properties; the problems concerning the derivation of a relation between the extraction and complex-properties of polydentate ligands and their structure have been combined in a separate section.

2. METHODS OF SYNTHESIS

a. The Arbuzov Reaction

This classical method of organophosphorus synthesis has been extensively used recently to obtain a wide variety of tertiary alkylenediphosphine dioxides. When a phosphine oxide containing a chloromethyl group is allowed to react with an ester of a secondary phosphinous acid, the dioxide of the tetrasubstituted methylenediphosphine is formed:

$$Ph_2P(O)-CH_2Cl + Ph_2P-OEt \rightarrow Ph_2P(O)-CH_2-PPh_2(O)$$

Tetraphenylbenzylidenediphosphine dioxide was synthesised similarly from α-chlorobenzyldiphenylphosphine oxide and ethyldiphenylphosphinite[4]. Derivatives of tetraphenylmethylenediphosphine with various substituents in

† We shall not consider the esters of alkylenediphosphonic acids, since a special review has been devoted to substances of this class[2].

the *meta*- and *para*-positions in the phenyl group were synthesised in the same way[5]:

$$(XC_6H_4)_2P(O)-CH_2-P(O)(C_6H_4X)_2,$$

where X = CH_3, CH_3O, Cl, Br, or CF_3.

The method of synthesising methylenediphosphine dioxides was extended to polymethylenepolyphosphine polyoxides, i.e. compounds containing several $-P(O)-CH_2-P(O)-$ units in the molecule[6-11]. The oxides of tertiary di(chloromethyl)-phosphine and tri(chloromethyl)-phosphine were introduced into the reaction with phosphorus(III) acid esters. In the first case the reaction proceeds via the mechanism

$$R-P(O)(CH_2Cl)_2 + 2EtOP(R')(R'') \rightarrow R'R''P(O)-CH_2-P(O)(R)-CH_2-P(O)R'R'' .$$

The intermediate products of the incomplete interaction of the initial components, $R'R''P(O)-CH_2-P(O)(R)CH_2Cl$, were also isolated.

The condensation of tri(chloromethyl)phosphine oxide with three ester molecules proceeds similarly:

$$(ClCH_2)_3P=O + 3EtO-P(R')(R') \rightarrow (R'R''PCH_2)_3P=O .$$

Compounds with R = CH_3, C_2H_5, $C_{12}H_{25}$, C_6H_5, C_2H_5O, or C_4H_9O and R′ and R″ = C_4H_9 or C_6H_5 were obtained.

Thus the chloromethyl group at the phosphorus atom, which contains a relatively passive halogen atom, is fairly reactive as regards the isomerisation of phosphorus(III) acids, which can be used successfully for the synthesis of a wide variety of polymethylenepolyphosphine polyoxides.

In the synthesis of ethylenediphosphine oxides one can employ as starting materials the β-chloroethyl esters of dialkyl- or diaryl-phosphinous acids, which on heating give rise to two products of the Arbuzov rearrangement; β-chloroethylphosphine oxide and ethylenediphosphine dioxide[12,13]:

$$R_2P-O-C_2H_4Cl \xrightarrow{t^\circ} R_2P(O)C_2H_4Cl + R_2P(O)C_2H_4P(O)R_2 .$$

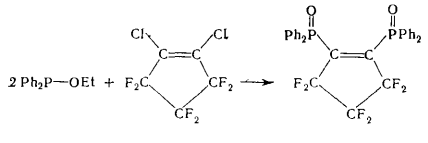
Depending on the conditions, the reaction proceeds preferentially via one pathway or the other. Thus isomerisation in solution promotes the formation of the monoxide and hinders the formation of the diphosphine dioxide. Presumably the β-chloroethyl ester of phosphinous acid initially undergoes intramolecular or intermolecular isomerisation and the resulting β-chloroethylphosphine oxide reacts like an alkyl halide with a second molecule of the β-chloroethyl ester via the mechanism of the Arbuzov rearrangement.

Diphosphine dioxides with ethylene and propylene bridges between the phosphorus atoms have been obtained from phosphinite esters and the corresponding dihalogenoalkanes[14]:

$$2(PhCH_2)_2P-OEt + Br(CH_2)_nBr \rightarrow (PhCH_2)_2P(O)-(CH_2)_n-P(O)(CH_2Ph)_2 .$$

(n = 2 and 3)

The reaction[15]



proceeds similarly.

In the above examples the Arbuzov isomerisation was used to bind two phosphorus-containing residues into the molecules of the alkylenediphosphine dioxide. The latter are also formed in the isomerisation of diphosphinous acid esters. For example, the Arbuzov rearrangement of a 1,4-dialkyl-substituted tetramethylenebis(diphenylphosphinite) in the presence of ethyl iodide leads to the formation of a tetraphenylalkylenediphosphine dioxide:

$$Ph_2-P-O-CHRCH_2CH_2CHR-O-P-Ph_2 \rightarrow Ph_2P(O)-CHRCH_2CH_2CHR-P(O)Ph_2 .$$

When the product of the reaction of ethylene glycol with chlorodiphenylphosphine is distilled, tetraphenylethylenediphosphine dioxide is formed immediately[16]. $Ph_2P(O)CH_2-CHPhOPPh_2$ also rearranges readily[17].

Alkylenediphosphine dioxides are also formed when phosphinamides react with diols with subsequent isomerisation on heating in the presence of catalytic amounts of dibromoethane[18]:

$$2R_2PNR'_2 + HO(CH_2)_nOH \rightarrow R_2P(O)-(CH_2)_n-PR_2(O) ,$$

where R = C_2H_5, C_4H_9, or C_6H_5 and n = 2, 3, 4, or 12.

b. The Michaelis–Bekker Reaction

The use of the magnesium salts of phosphorus(III) acids for the synthesis of alkylenediphosphine oxide was investigated by Kosolapoff[19]. The dioxides of tertiary alkylenediphosphines can be obtained in low yields by the reaction of halogenomagnesium salts of phosphinous acids with alkylenebis(toluene-*p*-sulphonates):[20]

$$2(Ph_2)POMgHal + Tos-O(CH_2)_nO-Tos \rightarrow Ph_2P(O)-(CH_2)_n-PPh_2(O) \quad (n=2, 3).$$

In the synthesis of tetrahexylethylenediphosphine and tetrahexylpropylenediphosphine dioxides Mrochek and Banks modified somewhat the method of isolating the product and increased the yield of the dioxide; or they also obtained tetrahexylbutylenediphosphine dioxide[21].

Tetraphenylmethylenediphosphine dioxide was synthesised by Kosolapoff and Struck[20] by treating halogenomagnesium phosphinite with methylene iodide or chloromethyldiphenylphosphine oxide[20]:

$$2Ph_2POMgCl + CH_2I_2 \rightarrow Ph_2P(O)-CH_2-PPh_2(O) .$$
$$Ph_2POMgCl + ClCH_2PPh_2(O) \rightarrow Ph_2P(O)-CH_2-PPh_2(O) .$$

Strunin et al.[22] and Kabachnik et al.[23] showed that halogenomagnesium salts of phosphinous acids, obtained by the reaction of organomagnesium compounds with dialkyl phosphites, react with alkylene dihalides, yielding alkylenediphosphine dioxides:

$$2R_2POMgX + X-(CH_2)_n-X \rightarrow R_2P(O)-(CH_2)_n-PR_2(O) ,$$

where R = C_6H_5, C_6H_{13}, or C_7H_{15}, X = Cl or Br, and n = 3 or 4.

Hays[24] achieved the alkylation of the halogenomagnesium salt of dimethylphosphinous acid with 1,2-dichlorobutane[24]:

$$2Me_2POMgBr + ClCH_2CHClCH_2Me \rightarrow Me_2P(O)-CH_2-CH(Et)-PMe_2(O) .$$

Tetracyclohexylethylenediphosphine dioxide was obtained by the reaction of sodium dicyclohexylphosphinite with dichloroethane[25].

c. Syntheses using Organometallic Compounds

Alkylenediphosphine dioxides can be obtained by the reaction of alkylenediphosphonic acid tetrachlorides with an excess of a Grignard monoreagent[26-29] or via the reaction of a phosphinic acid chloride with a Grignard direagent[30,31]:

$$Cl_2P(O)(CH_2)_nP(O)Cl_2 + 4RMgX \rightarrow R_2P(O)(CH_2)_nP(O)R_2$$
$$2R_2P(O)Cl + XMg(CH_2)_nMgX \rightarrow R_2P(O)(CH_2)_nP(O)R_2 \quad (n = 1-10)$$

In particular, dioxides with heteroatoms (O, S, and N) in the alkylene bridge between the phosphorus atoms were obtained in this way[26].

Richard and Banks described the synthesis of methylenediphosphine dioxides with symmetric and asymmetric structures from the lithio-derivatives of phosphine oxides and phosphinic acid chlorides[32]:

$$R_2PCH_3 \xrightarrow{BuLi} R_2PCH_2Li \xrightarrow{R_2P(O)Cl} R_2P(O)-CH_2-PR_2$$

Tetraphenylethylenediphosphine dioxide is formed when the molecules of the lithio-derivative of methyldiphenylphosphine oxide are dimerised under the influence of copper(I) chloride in tetrahydrofuran with subsequent treatment of the reaction mixture with oxygen[33]:

$$2(Ph_2)P(O)CH_2Li \xrightarrow{CuCl_2} Ph_2P(O)-CH_2CH_2-P(O)Ph_2$$

d. Syntheses based on Alkali Metal Phosphides

Certain syntheses of alkylenediphosphine dioxides involve the use of alkali metal phosphides, the properties and reactions of which have been extensively studied by Issleib[34]. Their reactions with dihalogenoalkanes can yield alkylenediphosphines, whose oxidation leads to the formation of alkylenediphosphine dioxides[35-37] (for $n = 1$ or 2, the dioxides are formed only from diphenylphosphide; in other cases diphosphyls were obtained[38]):

$$2R_2PM + X(CH_2)_nX \rightarrow R_2P-(CH_2)_n-PR_2 \xrightarrow{O_2} R_2P(O)-(CH_2)_n-P(O)R_2,$$

where R = C_2H_5, C_6H_{11}, or C_6H_5, $n = 1-6$, and M = Na or K.

Primary phosphides react similarly:

$$2RPHNa + Cl(CH_2)_nCl \rightarrow RPH(CH_2)_nPHR$$

The secondary alkylenediphosphines obtained in this way were converted by metallation into dilithioalkylene diphosphides, the interaction of which with alkyl halides followed by oxidation leads to the dioxides of mixed tertiary alkylenediphosphines[39,40]:

$$R_2P-(CH_2)_n-PR_2 \xrightarrow{Li} LiRP-(CH_2)_n-PRLi \xrightarrow{2R'X} R'RP-(CH_2)_n-PRR' \xrightarrow{O_2} R'RP(O)-(CH_2)_n-P(O)RR'$$

e. Cleavage of Phosphonium Salts

The formation of a butylenediphosphine dioxide from a diphosphonium salt on treatment with an excess of sodium butoxide has been described[41]:

$$[Ph_3P(CH_2)_4PPh_3]^{2+} \rightarrow Ph_2P(O)-(CH_2)_4-P(O)Ph_2$$

Petrov et al. synthesised the dioxides of tertiary diphosphines by alkylating dialkyl(aryl)(hydroxymethyl)-phosphines with dihalogenoalkanes and subsequent dehydroxymethylation of the resulting diphosphonium salts with sodium hydroxide and the oxidation of the alkylenediphosphines formed[42]:

$$2R_2PCH_2OH + X(CH_2)_nX \rightarrow [R_2P(CH_2OH)-(CH_2)_n-P(CH_2OH)R_2]^{2+}\,2X^- \xrightarrow{NaOH}$$
$$\rightarrow R_2P-(CH_2)_n-PR_2 \xrightarrow{H_2O_2} R_2P(O)(CH_2)_nP(O)R_2$$

The starting materials used were diheptyl-, dibutyl-, and diphenyl-(hydroxymethyl)phosphines, methylene iodide, and 1,2-dibromoethane; the yields of the alkylenediphosphine dioxides were high.

Horner et al. obtained the dioxides of tetraphenylalkylenediphosphines by heating chlorodiphenylphosphine with $Br(CH_2)_nBr$, where $n = 2$, 3, 4, or 6, or with $ClCH_2C_6H_4.CH_2Cl$ and subsequent hydrolysis of the intermediate alkylenebis(dihalogenophosphoranes).[43]

Similar syntheses was achieved by Tsivunin and Kamai and their coworkers from chlorodiethylphosphine; apart from dibromoalkanes, dichloromethyl ether was introduced into the reaction[44]. Tetramethylmethylenediphosphine dioxide was obtained from chlorodimethylphosphine and dibromomethane with subsequent decomposition by butyl alcohol[45].

Pyrolysis of (2-hydroxyethyl)diphenylphosphine leads to the formation of tetraphenylethylenediphosphine dioxide, probably via an intermediate dimeric diphosphonium base[46]:

$$Ph_2PC_2H_4OH \rightarrow Ph_2P^+(CH_2CH_2)_2P^+Ph_2\,2OH^- \xrightarrow{330^\circ} Ph_2P(O)CH_2CH_2P(O)Ph_2$$

f. Reactions Involving the Addition of Organophosphorus Compounds with a P–H Group to Multiple Bonds

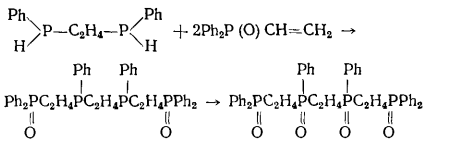
Organophosphorus compounds with a mobile hydrogen atom attached to a multiple bond have been used successfully to synthesise alkylene derivatives with two phosphorus atoms. The addition of diphenylphosphine oxide to diphenylvinylphosphine oxide leads to $Ph_2P(O)C_2H_4P(O)Ph_2$.[47] The reaction with α-chlorovinyldiphenylphosphine oxide proceeds via the following mechanism[4]:

$$Ph_2P(O)-CCl=CH_2 + Ph_2P(O)-H \rightarrow Ph_2P(O)-CHCl-CH_2-PPh_2(O) \xrightarrow{-HCl} Ph_2P(O)-CH=CH-PPh_2(O)$$

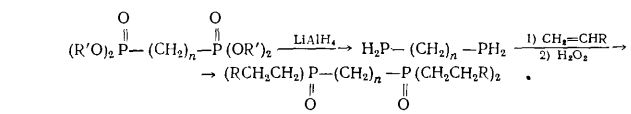
After dehydrochlorination, the *trans*-isomer of diphosphine dioxide is formed in this case (the *cis*-isomer was synthesised from Ph_2PLi and *cis*-dichloroethylene with subsequent oxidation[48]).

Alkylenediphosphines can be used as the bifunctional nucleophilic components in addition to an activated double bond. Hexaphenyltriethylenetetraphosphine tetroxide was

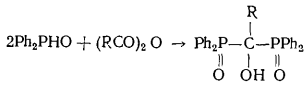
obtained by the reaction of ethylenediphenyldiphosphine with diphenylvinylphosphine oxide and subsequent oxidation[49]:



Maier[50] achieved the synthesis of alkylenediphosphine dioxides reducing alkylenediphosphonate esters to primary alkylenediphosphines with their subsequent addition to olefins and oxidation:



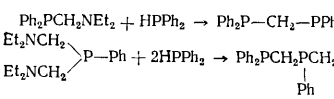
Davidson et al. described the reaction of diphenylphosphine oxide with carboxylic acid anhydrides, which apparently proceeds via a stage involving the addition of phosphine oxide to the C=O bond[51]:



where R = CH_3 or $C_6H_5CH_2CH_2$. The resulting hydroxyalkylidenediphosphine dioxides readily isomerise on heating via a mechanism of the type of the phosphonate–phosphate rearrangement.

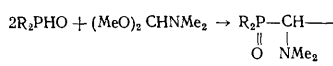
g. Other Methods

An interesting method for the formation of the P–C–P bond system was proposed by Maier on the basis of the reaction of phosphines containing the aminomethyl group with secondary phosphines[52]:



The oxidation of the products leads to the corresponding di- and tri-oxides.

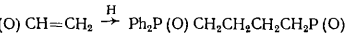
Gross and Costisella achieved the synthesis of the dioxides of amino-substituted methylenediphosphines by the reaction of the acetal or thioacetal of dimethylformamide with secondary phosphine oxides[53–56]:



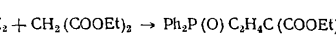
where R = C_4H_9 or C_6H_5.

Certain syntheses of the dioxides of tertiary alkylenediphosphines applicable in specific instances have been described.

Tetraphenylbutylenediphosphine dioxide has been obtained by the reductive dimerisation of diphenylvinylphosphine oxide (in aqueous acetonitrile with a platinum anode and a mercury cathode)[57]:

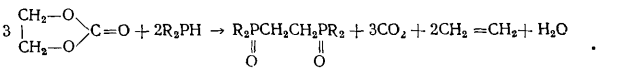


The interaction of malonic ester with two moles of diphenylvinylphosphine oxide proceeds as follows[47]:



Tetraphenylmethylenediphosphine dioxide has been obtained by the alkaline hydrolysis of methylenebis(diphenylphosphine-*N*-phenylimide)[58].

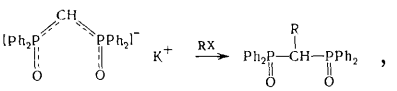
The formation of ethylenediphosphine dioxides has been observed in the reaction of dialkyl- and diaryl-phosphines with cyclic carbonic acid esters[59]:



h. Reactions of Alkylenediphosphine Dioxides

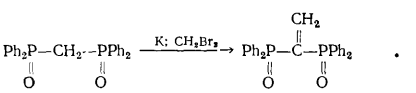
The reactions of diphosphine dioxides leading to changes in the hydrocarbon groups attached to the phosphorus atoms and proceedings without the dissociation of the C–P bonds, i.e. with retention of the initial structure of the tertiary alkylenediphosphine dioxide, are known.

Methylenediphosphine dioxides readily form metal salts on treatment with alkali metals or their hydrides. These salts are highly reactive and are used to obtain various derivatives substituted in the methylene bridge. Alkylation of the potassium salt of tetraphenylmethylenediphosphine dioxide by alkyl halides yielded *C*-alkylated products with substituents in the methylene group[60]:

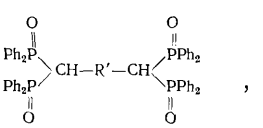


where R = C_2H_5, C_4H_9, C_6H_{13}, $C_{12}H_{25}$, $CH_2{=}CHCH_2$, or $CH{\equiv}CCH_2$.

The analogous reaction of tetraphenylmethylenediphosphine dioxide with methylene bromide leads to vinylidenediphosphine dioxide, which is probably formed as a result of the dehydrobromination of the bromomethyl-substituted dioxide by the initial potassium salt:



In the alkylation of the potassium salt of tetraphenylmethylenediphosphine dioxide by carbon tetrachloride, tetraphenyldichlorovinylidenediphosphine was obtained. The reaction of this salt with 1,6-dibromohexane and *p*-xylylene dibromide yields the corresponding octaphenylalkylenetetraphosphine tetroxides[60]:

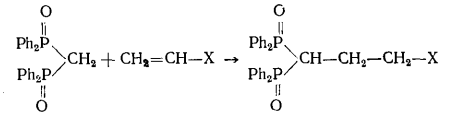


where R′ = $(CH_2)_6$ or n-$CH_2C_6H_4CH_2$.

The reaction with 1,5-dibromopentane under these conditions results in the formation of tetraphenylcyclohexylidenediphosphine dioxide.

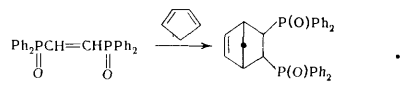
Halogenation of tetraphenylmethylenediphosphine dioxide with bromosuccinimide and thionyl chloride in the presence of azoisobutyronitrile yielded the corresponding monohalogeno-products; when the potassium salt of the dioxide is treated with iodine, the iodo-product is formed[61].

Tetraphenylmethylenediphosphine dioxide undergoes the Michael reaction in the presence of alkaline agents: its addition to ethyl acrylate, diphenylvinylphosphine oxide, and diethyl vinylphosphonate has been achieved[61]:

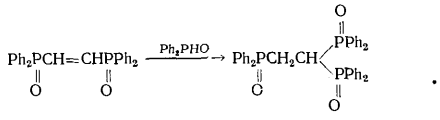


where X = C_2H_5OCO, $(C_6H_5)_2P(O)$, or $(C_2H_5O)_2P(O)$.

The *cis*- and *trans*-isomers of tetraphenylvinylenediphosphine dioxide undergo the Diels–Alder reaction with cyclopentadiene and are converted into the corresponding stereoisomers of norbornenylenediphosphine dioxide[62]:



The addition of diphenylphosphine oxide to phenylvinylenediphosphine dioxide leads to the trioxide of hexaphenyl-1,1,2-ethylenetriphosphine (which is also formed when Ph_2PHO reacts with trichloroethylene in the presence of triethylamine)[4]:



Tetracyclohexylmethylenediphosphine has been obtained by the hydrogenation of tetraphenylmethylenediphosphine dioxide over a platinum catalyst[63].

3. EXTRACTION PROPERTIES

The first reports of studies on polydentate neutral organophosphorus complex-forming agents dealt with tetraalkyl esters of alkylenediphosphonic acid[64]. Although compounds of this type are not in fact considered in this review, it is nevertheless useful to mention briefly certain investigations of their extraction properties, since relations common to alkylenediphosphine dioxides operate here too.

The study of the extraction of zirconium, yttrium, and certain lanthanides by tetra-n-butyl ethylenediphosphonate revealed its high extraction capacity[65]. Similar results were obtained in the extraction of thorium and uranium nitrates[66]. Siddal[67], who studied the properties of tetrabutyl alkylenediphosphonates $(BuO)_2P(O)-(CH_2)_n-P(O).(OBu)_2$, where n = 1, 2, 3, or 4, in the extraction of cerium, promethium, and americium, concluded that the bidentate compounds capable of forming chelates with metals (six- and seven-membered rings) are effective extracting agents.

A series of subsequent studies were devoted to the investigation of the compositions and structures of the complexes in the extraction of various metal salts by alkylenediphosphonate esters[68–73]. A common feature of all the studies quoted above is the conclusion that bidentate organophosphorus extractants have significantly more effective extraction properties (the partition coefficients are higher by a factor of 10–100) [67] than the monodentate extractants.

In the subsequent search for new highly effective neutral extractants, tetraalkyl(aryl)alkylenediphosphine dioxides were of considerable interest. These compounds have been attracting increasing attention: mainly the extraction of uranium from nitrate, chloride, and perchlorate solutions has been studied as well as the extraction of lanthanide and certain other elements. The mechanism of the extraction has been studied simultaneously with the aid of various physicochemical methods.

a. Extraction of Acids and Water

A number of investigations have been made[74–77] of the extraction of acids in which a relation between the extraction capacity of tetra-n-hexylalkylenediphosphine dioxides having the general formula $(C_6H_{13})_2P(O)-(CH_2)_n-P(O).(C_6H_{13})_2$, where n = 1, 2, 3, or 4, and the length of the hydrocarbon bridge between phosphoryl group was discovered.

Mrochek and Banks[75], who studied the extraction of nitric, hydrochloric, and perchloric acids at different concentrations with 0.05 M solutions of tetra-n-hexylalkylenediphosphine dioxides in 1,2-dichlorobenzene, showed that, with increase of the length of the hydrocarbon bridge, the extraction capacity of the dioxides increases in all cases. The degree of extraction of acids decreases in the following sequence as a function of the nature of the anion: $NO_3^- > ClO_4^- > Cl^-$.

The mechanism of the extraction of nitric acid by solutions of tetra-n-hexylmethylenediphosphine dioxide in benzene[76,77] and in carbon tetrachloride with formation of adducts has been studied most thoroughly:

$$H^+ + NO_3^- + S \overset{\bar{K}_1}{\rightleftarrows} HNO_3 \cdot S \ ,$$

$$[HNO_3 \cdot S] + H^+ + NO_3^- \overset{\bar{K}_2}{\rightleftarrows} (HNO_3)_2 \cdot S \ ,$$

where S is the extractant molecule. The effective extraction constants have been determined ($\bar{K}_1$ = 4.9 in CCl_4 and 9.8 in benzene and $\bar{K}_2$ = 0.18 and 0.35 in the two solvents respectively); with increase of the length of the bridge to n = 5, the constants become appreciably greater: $\bar{K}_1$ = 51 and $\bar{K}_2$ = 6.2.[76] However, it has been shown[77] that these equations to not describe the process fully: the constant $\bar{K}_1$ increases with increase of the extractant concentration above 0.05 M and also with decrease of the acid concentration. It has been suggested that this can be accounted for by the formation of solvates $HNO_3.mS$, where $m > 2$.

As for tri-n-butyl phosphate[78,79] and tri-n-butylphosphine oxide[80], in extraction from concentrated solutions the HNO_3 concentration in the organic phase exceeds the value for the stoichiometric composition $(HNO_3)_2.S$. Following Kertes and Platzner[81], the authors explained this by the extraction of undissociated acid.

The extraction of water by solutions of tetra-n-hexyl-, tetra-(2-ethylhexyl)-, and tetra-(3,3-dimethylbutyl)-alkylenediphosphines has been studied in chloroform[82,83] and it has been shown that complexes with water (monohydrates and dihydrates) are formed as a function of the length of the alkylene bridge in the ligand. This process competes with the extraction of salts and acids by the above compounds. Data for the distribution of water, obtained in the study of the infrared and NMR spectra, and the changes in the vapour pressure over the solutions established that, at concentrations of tetra-n-hexylmethylenediphosphine dioxide less than 0.02 M, the monohydrate is formed in the

organic phase. With increase of the extractant concentration in the organic phase, association complexes with a greater number of water molecules are produced.

b. Extraction of Uranium(VI)

The first studies in this field dealt with tetrabutyl methylenediphosphonate and tetrabutylethylene diphosphonate.

The series of studies by Banks and coworkers[74,75,82,84,85] were devoted to the investigation of a number of tetra-n-alkylalkylenediphosphine dioxides having the general formula $(Alk)_2P(O)(CH_2)_nP(O)(Alk)_2$, where $n = 1$, 2, 3, or 4. The n-hexyl, cyclohexyl, and 2-ethylbutyl substituents at the phosphorus atom were investigated. The results of the extraction of uranium(VI) and certain lanthanides from salt solutions in organic acids showed that these compounds are highly effective extractants, superior to the analogous phosphine monoxides.

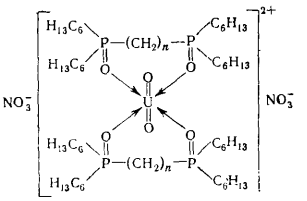
The extraction properties of tetraoctylethylenediphosphine dioxide in relation to uranyl nitrate were investigated by Laskorin and coworkers[86,87], who found that the extraction properties of this reagent depend in a complex manner on the composition of the aqueous phase.

The number of extractant molecules in the complex with uranyl nitrate has been determined[74] on the basis of the relation between the partition coefficients of uranium and the concentration of tetra-n-hexylmethylenediphosphine dioxide (S). It was found that the number is variable and depends on the ratio of the concentrations of the extractant and the salt. Thus, for equilibrium concentrations of the free extractant greatly exceeding the analogous concentration of the salt being extracted, the complex having the composition $UO_2(NO_3)_2.2S$ is formed in the organic phase. Under conditions close to saturation of the extractant, where the equilibrium concentration of the salt in the aqueous phase exceeds the equilibrium concentration of the free extractant, the complex $UO_2(NO_3)_2.S$ exists in the organic phase.

Analogous conclusions were reached in another study[85] where data were obtained, by a method involving the dilution of the extractant, for the compositions of the uranyl nitrate complexes with a number of alkylenediphosphine dioxides in solutions in 1,2-dichlorobenzene. The tetra-n-hexylalkylenediphosphine dioxides $(C_6H_{13})_2P(O)(CH_2)_n.(O)P(C_6H_{13})_2$ with $n = 1$ (DOHM), $n = 2$ (DOHE), $n = 3$ (DOHP), and $n = 4$ (DOHB) were investigated.

Examination of saturation and conductimetric data for solutions of alkylene diphosphine dioxides in 1,2-dichlorobenzene together with their infrared spectra for different ratios of the extractant and uranyl nitrate made it possible to determine the compositions and structures of the complexes extracted[85]. Thus the presence of the monosolvate $UO_2(NO_3)_2.S$ (the absorption band due to the P=O stretching vibrations is at 1136 cm^{-1}) and of the disolvate (the band at 1119 cm^{-1}) has been established for DOHM; similar solvates are also formed with DOHE (the 1124 and 1108 cm^{-1} bands).

The authors concluded that one or two NO_3^- groups in the disolvate with DOHM and DOHE are in the outer coordination sphere of the complex. This is confirmed by the greater intensity of the band due to the double degenerate antisymmetric stretching vibrations of the NO_3^- group (ν_3) at 1350 cm^{-1}, which is characteristic of the NO_3^- anion (D_{3h} symmetry) and by the sharp decrease of the intensity of the bands due to the allowed antisymmetric stretching vibrations at 1481–1520 cm^{-1} (ν_{3b}) and 1253–1290 cm^{-1} (ν_{3a}), which are characteristic of the covalently linked NO_3 group (C_{2v} symmetry)‡. Accordingly the disolvates with DOHM and DOHE have the following structure:

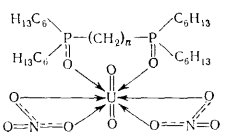


where $n = 1$ or 2.

The above data have been appreciably supplemented by studies on the structure of crystalline complexes of tetra-(2-ethylbutyl)methylenediphosphine (DOEBM) and tetracyclohexylmethylenediphosphine (DOCHM) dioxides with uranyl nitrate and thorium nitrate[84]. According to elemental analysis, the composition of the complexes isolated in the two cases is 1 : 1.

By analogy with the formation of complexes by uranyl nitrate with monodentate neutral organophosphorus compounds and bearing in mind that in the complexes with phosphate the NO_3^- group behaves as a bidentate ligand[88,96,97], the authors concluded that the NO_3 group plays a similar role in the complexes $UO_2(NO_3)_2.DOEBM$ and $UO_2(NO_3)_2.DOCHM$. This is in full agreement with the results of Mrochek et al.[85]

On passing to monosolvates, the nitrate ion anion virtually vanishes; accordingly the following structure has been attributed to the monosolvates $UO_2(NO_3)_2.DOHM$ and $UO_2(NO_3)_2.DOHE$:



where $n = 1$ or 2.

The infrared spectra of the complexes of DOHM and DOHE with uranyl nitrate, which are formed when the two reactants are in equimolar proportions, indicate the absence of water molecules from the coordination sphere of the complexes. In the spectra of the complexes where the ratio of the extractant and uranyl nitrate is 2 : 1 there is a band at 1620 cm^{-1} (O–H deformation vibrations), which indicates the presence of water molecules in their structure.

A very important result of the study of Mrochek et al.[74] is the demonstration of the bidentate coordination of uranyl nitrate to DOEBM and DOCHM on the basis of an investigation of the ^1H NMR spectra of the pure extractants and their complexes with uranyl nitrate. In the NMR spectra of solutions of DOEBM in $CDCl_3$ and of DOCHM in CCl_4 the protons of the methylene bridge give rise to a triplet, which indicates the equivalence of the two phosphorus atoms. When non-equivalent phosphorus atoms are present, as for example, in the di-(n-heptylphosphinyl)methylenephosphonic acid molecule $(n\text{-}C_7H_{15})_2P(O)CH_2(O)P(OH)_2$ the protons of the methylene bridge gave rise to a quartet signal. The fact that in the complexes $UO_2(NO_3)_2.DOEBM$ and $UO_2(NO_3)_2.DOCHM$ the protons of the CH_2 group give

‡ The infrared absorption bands of the NO_3 group under conditions where its covalent or ionic bond predominates in various compounds have been assigned in a number of studies[88–95].

rise to a triplet demonstrates the equivalence of the two phosphorus atoms and hence the bidentate coordination of the phosphoryl group.

The influence of certain electronic and steric factors on the extraction of uranium by tetraarylalkylenediphosphine dioxides has been studied. The results of these investigations are discussed below (see Section 5).

c. Extraction of Other Elements

The extraction of other elements by tetraalkyl(aryl)-alkylenediphosphine dioxides has also been investigated. The results characterise the selective properties of these substances. The qualitative data obtained by Parker and Banks[98] for the extraction of a number of elements from nitric and hydrochloric acids solution by tetra-n-hexylmethylenediphosphine dioxide are presented in the Table.

Characteristics of the extraction of a number of elements from nitric and hydrochloric acid solutions by $[n\text{-}C_6H_{13})P.(O)]_2CH_2$.

Medium	Quantitative extraction	Partial extraction	No extraction
1 M HNO_3	Au^{III}, Bi^{III}, Th, U^{VI}, Zr	Hg^{II}, Fe^{III}, Sm, Y, Mo^{VI}	Al, Ca, Cu, Ga, Pb, Mg, Ni, V, Zn
1 M HCl	Au^{III}, Bi^{III}, Th, U^{VI}, Hg^{II}, Mo^{VI}	Zr, Fe^{III}	Al, Ca, Pb, Zn, Ca, Cu, Fe^{II}, Ni, Sm, V, Y

In the extraction of thorium nitrate by tetraalkylmethylenediphosphine dioxides (S) [98] it was established that, in the presence of an excess of the extractant, complexes having the composition $Th(NO_3)_4.2S$ are formed in the organic phase. When there is a deficiency of the extractant, the complexes $Th(NO_3)_4.S$ are present in the organic phase.

Mrochek and Banks[75] quote comparative data for the extraction of praseodymium, neodymium, samarium, and thulium from nitric, hydrochloric, and perchloric acid solutions by tetrahexylalkylenediphosphine dioxides. After assessing the possibility of the employment of diphosphine dioxides as extractants for the separation of the lanthanides, the authors concluded that their selectivity is insufficient for this purpose.

An extensive study of the extraction properties of many tetraalkylmethylenediphosphine dioxides was carried out by O'Laughlin, Banks, and coworkers. Tetra-(n-hexyl)-methylenediphosphine dioxide proved to be extremely convenient as the stationary phase for the extraction chromatography of various metals, including the lanthanides[99]. A study of the extraction of samarium, thorium, and uranium from nitric acid solutions established that tetraalkylmethylenediphosphine dioxides with straight-chain alkyl groups are better extractants than compounds with branched side chains; compounds with branched side chains are relatively more effective for uranium(VI) than for thorium; the partition coefficients of samarium are much lower than those of thorium and uranyl[100].

The significant difference between the separation factors of lanthanide nitrates, chlorides, and perchlorates for separation with the aid of methylenediphosphine dioxides containing straight-chain and branched-chain alkyl groups (hexyl and 2-ethylhexyl) was explained by steric factors[101].

A detailed study of the separation of the lanthanides, thorium, and uranium with the aid of tetra-(n-hexyl)methylenediphosphine dioxide showed that the degree of separation increases appreciably with increase of the concentration of the nitric and hydrochloric acids[102]. Zirconium was isolated and determined in the presence of a large amount of niobium with the aid of the same dioxide used as the stationary phase[103]. In the extraction of the lanthanides from aqueous solutions of hydrochloric, nitric, and perchloric acids by tetraalkylmethylenediphosphine dioxides in carbon tetrachloride or 1,2-dichlorobenzene solution it was found that, tri- or di-solvates are formed, depending on the extractant concentration[104].

Alkylenediphosphine dioxides having the general formula $R_2P(O)-(CH_2)_n-P(O)R_2$, where $R = C_6H_{13}$ and $n = 1$, 4 or 5, have been used to extract tervalent actinides[105]. A study of the distribution of scandium between a nitric acid solution and a solution of tetraoctylethylenediphosphine dioxide in benzene established that the partition coefficient of scandium is directly proportional to the square of the extractant concentration in the organic phase and inversely proportional to the square of the concentration of hydrogen ions in the aqueous phase[106]. The extraction of cerium with the same extractant was also studied[107] and the same relations were established as in the experiments with scandium. In the extraction of radioactive europium(III) from hydrochloric acid solutions by mixtures of 2-thenoyltrifluoroacetone (S) with $(n\text{-}C_6H_{13})_2P(O)-(CH_2)_n-P(O).(C_6H_{13})_2$ (S') (where $n = 1$, 3, or 4) in cyclohexane adducts having the composition $Eu.S_3.S'$ are formed in the organic cyclohexane phase and synergism is observed[108].

An unusual instance of extraction of the lanthanides by tetraphenylethylenediphosphine dioxide was described recently[109,110]. Praseodymium, europium, and thulium are extracted from the $LiNO_3$–KNO_3 eutectic melt at 160°C. The organic phase is a mixture of biphenyl, *o*-terphenyl, and *m*-terphenyl in which the extractant concentration is 5×10^{-5} M. Two pairs of elements were separated: praseodymium–europium and praseodymium–thulium. In the extraction of americium, curium, and californium under analogous conditions using tetraphenylalkylenediphosphine dioxides $Ph_2P(O)-(CH_2)_n-P(O)Ph_2$, where $n = 2$, 3, or 4, as the extractants lower partition coefficients are observed than for praseodymium, europium, and thulium.

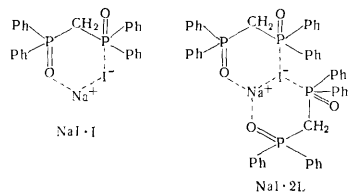
4. COMPLEX-FORMING PROPERTIES

a. Complexes with Alkali Metal Halides

The authors of the present review[111] established that methylenediphosphine dioxides form stable crystalline complexes with alkali metal iodides having the composition $2R_2P(O)CH(R')P(O)R_2.MX$.

Hewerson et al.[112], who oxidised tetraphenylmethylenediphosphine with hydrogen peroxide in acetone in the presence of sodium bromide, isolated the crystalline complex $[(PH_2P(O)CH_2P(O)Ph_2)_3Na]Br.3H_2O$, in which the sodium cation is chelated by three molecules of tetraphenylmethylenediphosphine dioxide with formation of a trigonal prism containing six oxygen atoms.

Yatsimirskii et al.[114] investigated the interaction of alkali metal halides with tetraaryl(alkyl)methylenediphosphine dioxides in non-aqueous solutions. They employed for this purpose conductimetric, spectrophotometric, interferometric, solubility, and other methods. The results obtained in the study of the formation of a sodium iodide complex with tetraphenylmethylenediphosphine dioxide[113] suggested that the entire NaI molecule (ion pair) is involved in the formation of complexes. At this stage of the investigation the hypothesis was put forward that the bond linking the iodide ion to the phosphorus atom can be formed partly as a result of the electrostatic interaction but is mainly due to the overlapping of the orbitals of the ion with the free non-bonding *d* orbitals of phosphorus. The complex formed can be stabilised by the inclusion in its composition of the alkali metal ion. There is then a possibility of the formation of a six-membered ring in which the alkali metal ion interacts electrostatically with the iodide ion and the oxygen atom on which a negative charge is localised. The ring can be built up also on the other side with formation of a condensed complex. The structures of the complexes NaI.L and NaI.2L might have been represented as follows according to this hypothesis:



NaI·I NaI·2L

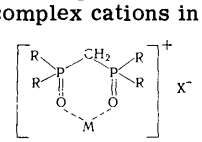
However, further study led to findings conflicting with this hypothesis. Thus, according to ^{31}P NMR data, the two phosphorus atoms are magnetically equivalent, while according to the hypothesis they are non-equivalent. The determination of the real structure of the complexes evidently requires further studies.

To elucidate the influence of the nature of the alkali metal halide on the type of its interaction with phosphine oxides a study has been made of the electrical conductivity of the MX–$Ph_2P(O)CH_2P(O)Ph_2$–acetonitrile system[114], and it has been found that, depending on the nature of the cation and anion in the MX molecule, complex formation can proceed in accordance with one of the following equations:

$$M^+ + X^- + nL \rightleftarrows MX \cdot nL \quad , \qquad (1)$$

$$MX + L \rightleftarrows [ML]^+ + X^- \quad . \qquad (2)$$

The electrically neutral complexes described above arise in the first case and complex cations in the second:



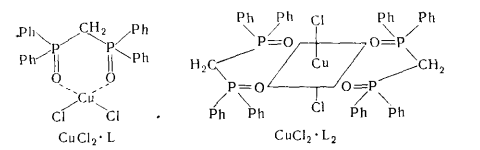
The formation of complexes of the type MX.L or $[ML]^+X^-$ obeys a specific relation: the most favourable conditions for the formation of electrically neutral complexes are created in systems containing a cation with a small radius and a high ionic potential and a large readily polarisable anion. The influence of the structure of phosphine oxides and of the nature of the substituents on the properties of the complexes formed has been studied. A quantitative estimate of the complex-forming properties of phosphine oxides has been made on the basis of the stability constants of their complexes with NaI (the electrically neutral complexes NaI.L) and LiCl {the positively charged complexes $[Li.L]^+$}.[115] The stability of the NaI.L complexes depends significantly on the nature of the substituent at the phosphorus atom. The phenyl group, which can behave both as an electron-donating and an electron-accepting agent, permits the formation of a more stable complex than, for example, the butyl group which behaves as an electron donor only or the butoxy-group which behaves more as an electron acceptor. The complex with an asymmetric dioxide proved to be the most stable.

The interaction of alkali metal halides with tetraalkyl-(aryl)alkylenediphosphine dioxides containing different numbers of methylene groups linking the phosphorus atoms[116], different substituents in the phenyl groups[117], and different substituents in the methylene bridge[118] has also been studied. The results of these investigations are discussed below (see Section 5).

b. Complexes with Copper and Other Metal Salts

The interaction of copper(II) chloride with tetraphenylmethylenediphosphine dioxide $Ph_2P(O)CH_2P(O)Ph_2$ in acetone leads to the formation of the complexes $CuCl_2.L$ and $CuCl_2(Ac)_2$, which can be isolated from solution[119]. At low ligand concentration in solution the product is the complex $[CuCl.L]^+$, while in the presence of an excess of the ligand the complex containing copper(II) chloride and the ligand in the proportions 1 : 2 is formed when the solutions are allowed to stand. The absorption spectrum of the 1 : 1 complex contains a charge-transfer band at 21 000 cm^{-1}; the 1 : 2 (M : L) complex does not exhibit such properties. The stability constant of the complex $[CuCl.L]^+$ was determined from spectrophotometric and conductimetric data.

The structures of the complexes formed can be represented schematically as follows:



$CuCl_2 \cdot L$ $CuCl_2 \cdot L_2$

In the $CuCl_2.L$ complex all four electron-donating atoms (two O atoms and two Cl atoms) are probably located in the same plane. In the $CuCl_2.2L$ complex the four oxygen atoms are probably located in the equatorial plane (the XV plane) and two chloride ions are above and below this plane.

An X-ray diffraction study of the crystalline copper(II) chloride complex with tetraphenylethylenediphosphine dioxide showed that it exhibits a very marked deviation from the ideal tetragonal symmetry[120]. Complexes of tetraphenylethylenediphosphine dioxide with cobalt halides have also been obtained. All the complexes are paramagnetic.

Certain complexes of organic copper(I) compounds (phenylcopper, tolylcopper, and others) with tetraphenylmethylenediphosphine and tetraphenylethylenediphosphine have likewise been isolated and characterised[121].

The interaction of copper(II) chloride with substituted tetraphenylmethylenediphosphines[117] and also the influence of the length of the chain between the phosphoryl groups on the complex-forming properties of alkylenediphosphine dioxides[116] were studied by Sheka, Yatsimirskii et al. The results of these investigations are discussed below (see Section 5).

In addition to the complexes of the copper salts, a study was also made of the formation of complexes with salts of other metals. The formation of stable 1:1 complexes of tin(IV) chloride and bromide with tetraphenylethylenediphosphine and tetraphenylbutylenediphosphine dioxides has been described[122]. Complexes having the following compositions

$MoOBr_3[Ph_2P(O)CH_2CH_2P(O)Ph_2]$,
$MoO_2Br_2[Ph_2P(O)CH_2CH_2P(O)Ph_2]$,
$MoOCl_3[Ph_2P(O)CH_2CH_2P(O)Ph_2]$,
$MoO_2Cl_2[Ph_2P(O)CH_2CH_2P(O)Ph_2]$,
$WO_2Cl_2[Ph_2P(O)CH_2CH_2P(O)Ph_2]$,
$WO_2Br_2[Ph_2P(O)CH_2CH_2P(O)Ph_2]$

have been synthesised by treating tetraphenylethylenediphosphine dioxide and molybdenum or tungsten hexacarbonyls with halogens, isolated, and characterised[123].

The complexes of tetraphenylmethylenediphosphine dioxide (L) with rhenium(I) carbonyl halides have been obtained and investigated: $Re(CO)_3L$, $Re(CO)_3LBr$, and $Re(CO)_3LCl$.[124] The formation of magnesium and calcium halide complexes with tetraphenylmethylenediphosphine dioxide (L) was established by studying the electrical conductivity of and ion transport in solutions of magnesium and calcium iodides and chlorides in acetonitrile. The complexes $[Mg.L]^{2+}$ and $[MgI.L]^+$ are formed with magnesium iodide, while the existence of the complexes $[Ca.L]^{2+}$ and $[CaCl.L_2]^+$ has been observed[125] for calcium chloride.

A spectrophotometric study of neodymium chloride solutions with tetraphenylmethylenediphosphine dioxide in butyl alcohol established that the complexes $NdCl_3.nL$ (n = 1 or 3) and $NdCl_3.nL_2$ (n = 1, 2, or 3) are formed in steps[126].

5. DEPENDENCE OF THE EXTRACTION AND COMPLEX-FORMING PROPERTIES ON THE STRUCTURE OF THE LIGANDS

Although the number of publications dealing with polydentate organophosphorus complex-forming agents has increased recently, problems such as the relation between the structure and stability of the complexes, the relation between structure and selectivity of ligand action, the relation between the stability constants of the complexes and the capacity for complex formation in heterogeneous media, as well as many other aspects have not been studied.

Certain general problems in the field of polydentate neutral organophosphorus complex-forming agents were investigated by the authors of the present review. It was of interest to discover the influence of the electronic effects of the environment of the active centre of the ligand on complex formation and also the role of steric and structural factors.

a. The Electronic Effects of Substituents

The dependence of the extracting capacity of tetraarylmethylenediphosphine dioxides $(RC_6H_4)_2P(O).CH_2P(O).(C_6H_4R)_2$ containing various substituents in the *meta*- and *para*-positions in the benzene rings (CH_3O, CH_3, Cl, Br, CF_3, etc.) was studied in relation to uranyl nitrate[127]. It was established by the method involving dilution of the extractant that the complexes $UO_2(NO_3)_2.3S$ and $UO_2(NO_3)_2.2S$ exist in the organic phase. The effective extraction constants were calculated for uranyl nitrate ($\overline{K}$) and a correlation between $\lg\overline{K}$ on the one hand and $\Sigma\sigma^{ph}$ and $\Sigma\sigma$ was established for the trisolvates. It was also shown that there is a linear relation between the extracting capacity of the dioxides and the pK defining their basicity. The effective extraction constant varies within wide limits: from 0.8×10^{10} (for the p-MeO substituent) to 70 ± 20 (for the p-CF_3 substituent).

The formation of complexes with copper(II) chloride has also been studied for the same series of substitued dioxides[117]. The stepwise stability constants of the complexes $[CuCl.L]^+$ were determined and a correlation was established between these quantities and the σ constants of the substituents and the basicity (pK_a) of the ligands. The stability constants are higher the weaker the electron-accepting properties of the substituents: $\lg\beta_{ML}$ varies from 3.74 (for p-CF_3) to 4.62 (for p-MeO).

Next the complex-forming properties of tetraphenylmethylenediphosphine dioxides with a substituent in the methylene bridge, $Ph_2P(O)-CHR-P(O)Ph_2$, were investigated. It was found that in the case of uranyl nitrate either the trisolvates or disolvates exist in the organic phase. The effective extraction constants were calculated for the trisolvate complexes and, although they were found to vary for dioxides with different substituents in the bridge, they nevertheless remained within the limits of the same order of magnitude. On the other hand, as shown above, for dioxides with substituents in the phenyl groups these values vary in the range of 4–5 orders of magnitude. The formation of complexes of copper(II) chloride was studied on the basis of stability constants calculated from spectrophotometric data. It was shown that the bridge-substituted tetraphenylmethylenediphosphine dioxides (R = Cl, Br, I, C_6H_5, or $C_6H_5CH_2$), without functional groups in the substituents capable of a donor-acceptor interaction with the metals, form complexes of the same type whose stability is determined mainly by the inductive properties of the substituents. On the other hand, in the presence of substituents containing functional groups [R = CH_2CH_2COOH, $CH_2CH_2P(O)Ph_2$, $CH_2CH_2P(O).(OH)_2$, etc.], which may be involved in complex formation, the compositions structures, and stabilities of the complexes formed are altered.

b. Effect of the Length of the Bridge Between the Phosphorus Atoms

The phosphoryl groups in alkylenediphosphine dioxide molecules are electronegative and exert on one another an influence which weakens the complex-forming capacity of the dioxides. An increase of the distance between the phosphoryl groups reduces their mutual influence. On the other hand, the dimensions and stability of the rings of the chelate compounds formed depend on the number of methylene units in the bridge. Allowance for these factors makes it possible to suggest that the length of the alkylene bridge between the phosphoryl groups can have a significant influence on the complex-forming properties of the dioxides.

Mrochek et al. demonstrated the influence of the alkylene bridge on the composition of the complexes formed in the extraction of uranyl nitrate by tetrahexylalkylenediphosphine dioxides[85]:

$$(C_6H_{13})_2P(O)-(CH_2)_n-P(O)(C_6H_{13})_2,$$

where n = 1, 2, 3, or 4. The dioxide with the methylene bridge exhibits the highest extracting capacity in this series[75]. Laskorin et al.[128] found that the maximum partition coefficient in the extraction of uranium from nitric

and hydrochloric acid solutions by di- and poly-oxides is observed for tetraoctylethylenediphosphine dioxide; a further increase of the length of the bridge between the phosphorus atoms leads to a monotonic decrease of the partition coefficients of uranium.

The influence of the number of methylene units between the phosphoryl groups on the complex-forming[116] and acid–base properties[129] of alkylenediphosphine dioxides containing aryl or alkyl substituents at the phosphorus atoms has been studied. The dioxides of two homologous series were investigated as ligands:

$$Ph_2P(O)-(CH_2)_n-P(O)Ph_2,$$

where $n = 1 - 3$, and

$$Bu_2P(O)-(CH_2)_n-P(O)Bu_2,$$

where $n = 1-6$.

The results of potentiometric titration of the dioxides[129] in nitromethane led to the hypothesis that the protonation of the dioxides with methylene and ethylene bridges proceeds via the formation of rings with an intramolecular hydrogen bond involving both phosphoryl groups. In the presence of a larger number of methylene units the ring probably ruptures and the second phosphoryl group is protonated.

The interaction of the same alkylenediphosphine dioxides with alkali metal halides and copper(II) chloride was studied on the basis of the changes in the electrical conductivities of solutions of the salts following the addition of the ligand[116]. As already mentioned, neutral complexes are formed with alkali metal iodides in acetonitrile, while the chlorides give rise to positively charged complexes. Dioxides with a methylene bridge ($n = 1$) have the most marked complex-forming capacity, the interaction with the salts being reduced in parallel with the increase of the ring size as the number of methylene groups between the phosphorus atoms increases. For tetrabutylalkylenediphosphine dioxides with $n = 4$ or 6, an enhancement of the complex-forming effect is observed, probably owing to the rupture of the chelate ring, and the addition of two MX molecules to the dioxide molecule (both phosphoryl groups act independently). For tetraphenylalkylenediphosphine dioxides, an increase of n leads to a sharp weakening of the complex-forming properties.

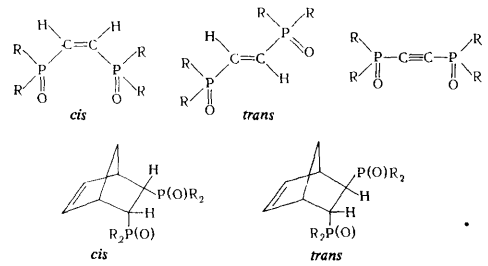
The study of the formation of complexes of copper(II) chloride by spectrophotometric and conductimetric methods showed that tetrabutylmethylenediphosphine and tetrabutylethylenediphosphine dioxides ($n = 1$ or 2) form complexes having the same composition $[CuCl.L]^+$, while for $n = 3$, 4 or 6 ring formation does not occur and the two phosphoryl groups act separately; one cannot rule out the possibility of the formation of polymeric forms of the complexes.

c. Stereochemical Factors

The above data concerning the complex-forming properties of alkylenediphosphine dioxides make it possible in many cases not only to understand but also to predict the nature of the complex formation reaction with particular metals. These considerations apply mainly to the stability of the complexes formed and to the possibility of controlling it largely by varying the electron-donating capacity of the active centre of the ligand.

The problems of the selectivity of the action of the complex-forming agents are a no less interesting and important aspect of the investigation of their properties, since the solution of the problem of selective complex formation is of exceptional significance. However, the principles of creating a complex-forming agent with a high selectivity in relation to the specified metal are still far from being elucidated. Certain studies on these lines were undertaken by the present authors, who began with the hypothesis that the inclusion in the molecule of the complex-forming agent of fragments preventing the free rotation of the individual units and fixing the disposition of the electron-donating atoms would increase the selectivity and efficiency of the complex-forming agent.

This hypothesis was tested by investigating the extraction and complex-forming properties of alkylenediphosphine dioxides with a "rigid" structure, containing a vinylene bridge or a triple bond between the phosphoryl groups: the dioxides of the *cis*- and *trans*-isomers of tetraphenylvinylenediphosphine; tetraphenylethynylenediphosphine dioxide; bicyclic adducts of dioxides containing *cis*- and *trans*-vinylene bridges with cyclopentadiene:



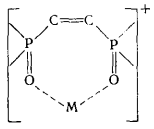
The extraction capacity was studied in relation to nitric acid and uranyl nitrate[130]. It was shown that the partition coefficient of uranyl nitrate is higher by three order of magnitude when the *cis*-isomer of the dioxide with the vinylene bridge is used compared with the dioxide containing an ethylene bridge. Conversely, by fixing the P=O groups in the *trans*-positions, the degree of extraction is reduced to the level characteristic of the corresponding monoxide. The adducts of the *cis*- and *trans*-dioxides with cyclopentadiene behave similarly. The lowest extraction capacity is characteristic of the compound with the ethynylene bridge. The formation of rings is impossible with *trans*-isomers of the dioxide with the ethynylene bridge (the disposition of the atoms in P–C≡C–P is linear). The appreciably enhanced extraction of uranyl nitrate by *cis*-tetraphenylethynylenediphosphine dioxide compared with dioxides containing methylene and ethylene bridges can be attributed to a rigid steric distribution of the phosphorus atoms because, on the one hand, the entropy component of the free energy changes, and, on the other, the distance between the oxygen atom decreases. Possibly it becomes optimal as a result of the formation of rings with uranyl nitrate. Similar results were obtained in a study of the extraction of molybdenum[131].

Thus steric factors have a very significant influence on the extraction properties of the complex-forming agent.

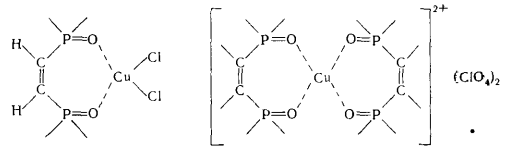
Analogous data were secured in a study of the influence of steric factors on the complex-forming properties of alkylenediphosphine dioxides[132]. The influence of the mutual disposition of the phosphoryl groups in vinylenediphosphine dioxides on the properties of the complexes which they form with certain alkali and transition metal halides was studied. Methylenediphosphine dioxides form electrically neutral cyclic complexes with lithium and sodium iodides as a result of the incorporation in the complex of the ion pair M^+I^-.

The *trans*-isomers of dioxides with a vinylene bridge also form electrically neutral complexes, which shows that the *trans*-disposition of phosphorus atoms apparently makes it possible to form monomeric complexes with the ion pairs M^+I^-.

The interaction of the *cis*-isomer with the same salts results in the formation of positively charged complexes—in this case the cation adds to the oxygen atoms of both phosphoryl groups:

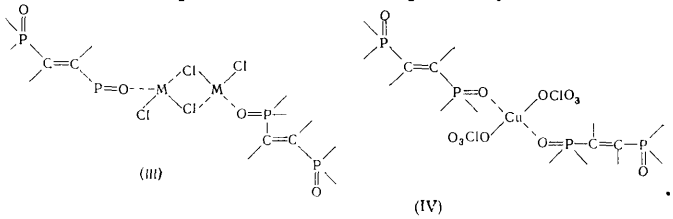


Complexes of the isomeric vinylenediphosphine dioxides have been obtained with cobalt(II) and copper(II) salts. On the basis of reflection and infrared spectroscopic data, structures (I) and (II) were attributed to the crystalline complexes of the *cis*-isomers having the composition $CuLCl_2$ and to the complexes $CuL_2(ClO_4)_2$ respectively:



(I) (II)

Structures (III) and (IV) are most probable for the cobalt(II) and copper(II) complexes with the *trans*-isomers and for the complex $CuL_2(ClO_4)_2$ respectively:



(III) (IV)

Coordination compounds of the dioxides with nickel chloride were obtained by fusing the components at the melting points of the dioxides. The chlorides of the transition metals investigated form 1 : 1 coordination compounds and the perchlorates form 1 : 2 complexes.

The absorption spectra of cobalt complexes show that the absorption band due to the *d*–*d* transition is in the region characteristic of tetrahedral complexes. In the spectra of the copper complexes the band of the *d*–*d* transition is in the near infrared, which suggests that the symmetry of the chromophore in the copper complexes is intermediate between tetrahedral and square planar. At high temperatures the complexes of nickel chloride have spectra characteristic of tetrahedral complexes, while at room temperature the structure of these complexes becomes largely octahedral, which is confirmed both by the spectra and the magnetic moments.

The band due to the vibrations of the free P=O group persists in the infrared spectra of the complexes with the *trans*-isomers of the dioxides and a new band appears, which can be attributed to the vibration of the P=O group bound to the metal. In this case the dioxide behaves as a monodentate ligand, i.e. it combines with the metal via one phosphoryl group. In the spectra of the complexes with the *cis*-isomer the bands due to the vibrations of the P=O group are displaced, which implies that both phosphoryl groups are linked to the metal and the ligand is bidentate.

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The Azidoazomethine-Tetrazole Tautomerism

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The review deals with the literature on the azidoazomethine-tetrazole tautomerism of condensed tetrazoles with a detailed consideration of the influence of the structure of the condensed tetrazoles, the nature of the substituents, solvents, and temperature on the state of the azidoazomethine-tetrazole equilibrium.
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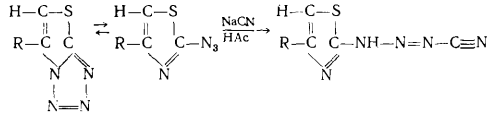
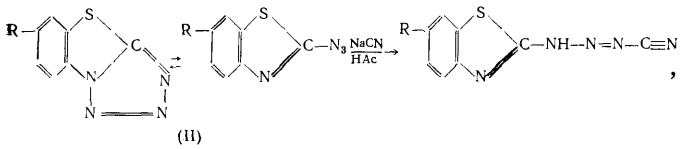
I. INTRODUCTION

A number of studies have been carried out since 1951 on the synthesis and properties of certain condensed tetrazoles[1-24]. The chemistry and fine structure of tetrazolo[5,1-*b*]benzothiazoles and thiazolo[2,3-*e*]tetrazoles were investigated in greatest detail. The studies led to the conclusion that the tetrazole ring condensed with an aromatic heterocycle via the $N_{(1)}-C_{(5)}$ bond is as a rule less stable than 1,5-disubstituted tetrazoles. In many cases it is opened at the $N_{(1)}-N_{(2)}$ bond with formation of the isomeric azidoazomethine derivative. Similar transformations in the series of tetrazolo[5,1-*b*]benzothiazoles and thiazolo[2,3-*e*]tetrazoles frequently occur on heating or dissolution of the substance and following the introduction of electron-accepting substituents into the heterocycle. Therefore, while retaining the properties of 1,5-disubstituted tetrazoles, they enter into reactions characteristic of azides, which was first demonstrated in a number of investigations[1,4,7-10,13,16,18,19,21]. For example, like azides, tetrazolo[5,1-*b*]benzothiazoles and thiazolo[2,3-*e*]-tetrazoles condense with sodium or potassium cyanide to form benzothiazol-2-yl- and thiazol-2-yl-cyanotriazenes respectively[4,19]:



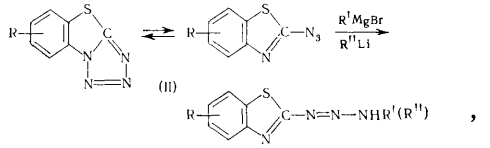
(I)

where R = Me or Ph;



(II)

where R = H, Me, MeO, EtO, F, Cl, or Br. A very interesting relation between condensed tetrazoles and organomagnesium halides and organolithium compounds has been described[1,4,7,13,18,19,21]. It was found that all tetrazolo[5,1-*b*]benzothiazoles, with the exception of the 8-methyl derivative, readily react (like azides) in ether with phenylmagnesium bromide and phenyllithium with formation of phenyl(benzothiazol-2-yl)triazenes:



(II)

where R = H, 6-Me, 6-Cl, 4-Cl, or 6-MeO, R′ = Ph, Bu, Me, or $PhCH_2$, and R″ = Ph or Bu.

8-Methyltetrazolo[5,1-*b*]benzothiazole does not react with phenylmagnesium bromide and phenyllithium. Alkylmagnesium halides and alkyl-lithium compounds are not involved in the formation of aliphatic-aromatic triazenes even on refluxing the reaction mixture in benzene solution. Under these conditions, the initial tetrazoles were isolated in almost quantitative yields[19,21].

On the other hand, 2-azido-4-chlorobenzothiazole, which is isomeric with 8-chlorotetrazolo[5,1-*b*]benzothiazole, forms triazenes with organomagnesium halides regardless of the nature of the organic group[19].

Thiazolo[2,3-*e*]tetrazoles form the corresponding triazenes with phenylmagnesium bromide, phenyl-lithium, and alkylmagnesium halides readily only in the case of the 6-phenyl derivatives[19].

It is interesting that the replacement of the electronegative phenyl group in 6-phenylthiazolo[2,3-*e*]tetrazole by the electropositive methyl group leads to the loss of capacity for the formation of triazenes in the reaction with organometallic compounds.

It has been shown that tetrazolo[5,1-*a*]pyridine does not form triazenes when acted upon by organometallic compounds or sodium and potassium cyanides[19,21]. On the other hand, it has been stated[25] that pyrido[5,1-*a*]tetrazole reacts with triphenylphosphine like azides[18], forming triphenylphosphazo-compounds. The behaviour of tetrazolo[5,1-*b*]benzothiazole and thiazolo[2,3-*e*]tetrazole in relation to phosphines is similar[26].

The reaction of tetrazolo[5,1-*o*]benzothiazoles with 3-methyl-1-phenylpyrazol-5-one and its derivatives has been described[9] and it has been shown that these reactions proceed similarly to the reactions of phenyl azide.

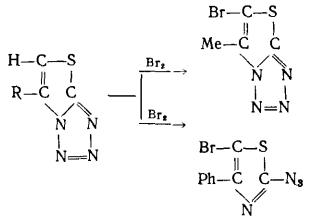
On the other hand, condensed tetrazoles are much more resistant to chemical agents (concentrated acids, oxidising agents) and to light than azides[1,7,10,16,17]. The oxidation of tetrazolo[5,1-*b*]benzothiazole derivatives does not

involve the tetrazole ring. For example, the oxidation of 6-methyltetrazolo[5,1-*b*]benzothiazole leads to the formation of tetrazolo[5,1-*b*]benzothiazole-6-carboxylic acid[10,17].

Dissolution of thiazolo[2,3-*e*]tetrazoles and tetrazolo-[5,1-*b*]benzothiazoles in concentrated inorganic acids leads to the protonation of the tetrazole ring, and, when they are treated with alkylating agents, quaternary tetrazolium salts are formed[14,17].

The isomerisation of 2-azido-4-chlorobenzothiazole to 8-chlorotetrazolo[5,1-*b*]benzothiazole on treatment with sulphuric acid or dimethyl sulphate has been noted[14,17].

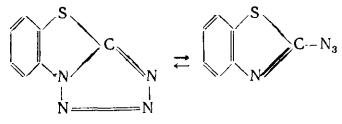
Avramenko, Pochinok, Skopenko, and others[10,17,20,23,24] investigated the halogenation, sulphonation, chlorosulphonation, nitration, and substitution with thiocyanate of thiazolo[2,3-*e*]tetrazoles and tetrazolo[5,1-*b*]benzothiazoles. The halogenation of 6-methylthiazolo[2,3-*e*]tetrazole and its substitution with thiocyanate involve the 5-position of the condensed system and lead to the formation of 5-bromo-6-methyl- and 6-methyl-5-thiocyanato-thiazolo[2,3-*e*]tetrazoles. The corresponding reactions with 6-phenylthiazolo[2,3-*e*]tetrazole proceed similarly at the 5-position. However, the tetrazole ring is opened under the influence of the electronegative phenyl substituent and the reaction products are the isomeric azido-derivatives:



where R = Me or Ph.

The sulphonation, chlorosulphonation, and nitration of 6-phenylthiazolo[2,3-*e*]tetrazole also proceed at the 5-position. The introduction of powerful electron-accepting substituents results in the formation of the isomeric 2-azido-derivatives[17,20,24]. It has been shown[23] that nitration of tetrazolo[5,1-*b*]benzothiazole takes place at the 7-position of the condensed system and the nitration product has the structure of 2-azido-5-nitrobenzothiazole.

In view of the dual nature of the condensed tetrazoles investigated (on the one hand they exhibit the properties of azides and on the other they are much more stable than organic azides and behave like true tetrazoles), Pochinok[2,3] suggested for the first time in 1956 the occurrence of the azidoazomethine–tetrazole tautomerism for condensed tetrazoles:



(II)

It follows from the reactions of various condensed tetrazoles with organometallic compounds, sodium or potassium cyanide, and phosphines that the course of the reaction depends on the state of the azidoazomethine–tetrazole equilibrium, which is influenced by the nature of the substituent in the heterocycle and by the chemical nature of the reagent acting upon the condensed tetrazole.

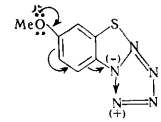
Subsequently the phenomenon of the azidoazomethine–tetrazole tautomerism was demonstrated exactly with the aid of physical research techniques, particularly infrared and NMR spectroscopy.

In 1959 Reynolds et al.[27] and also Boyer and Miller[28] concluded on the basis of spectroscopic studies on condensed tetrazoles that the azidoazomethine–tetrazole tautomerism is possible for some condensed tetrazoles. Infrared spectroscopic data led Boyer and Miller[28] to the hypothesis that tetrazolo[5,1-*b*]benzothiazole is a condensed system in the crystalline state, while in solution it is an equilibrium mixture of the azide and tetrazole forms. In 1961 Sheinker et al.[29] published the results of an infrared spectroscopic study of tetrazolo[5,1-*b*]benzothiazole, which confirmed the earlier conclusions. Furthermore, they observed for the first time that the tetrazolo[5,1-*b*]-benzothiazole ⇌ 2-azidobenzothiazole equilibrium occurs also in the melt[29].

Separate studies on the azidoazomethine–tetrazole tautomerism of tetrazolo[5,1-*b*]benzothiazole, thiazolo[2,3-*e*]tetrazole, and their derivatives were also carried out by infrared spectroscopy[10,11,16,17,20]. The phenomenon of the azidoazomethine–tetrazole tautomerism was likewise observed for other condensed tetrazoles. There are literature data for the azidoazomethine–tetrazole tautomerism of tetrazolopyridine[28,30,31], tetrazolopyrimidines[32-35], tetrazoloquinazoline[36,37], etc.

Condensed tetrazoles have been described in a number of reviews dealing with the chemistry of tetrazoles[38-40]. The reviews by Tisler[41] and Butler[42] on certain aspects of the azidoazomethine–tetrazole tautomerism were published in 1973.

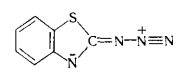
It has been shown[11,14,17,20,33,34] that the state of equilibrium between the azide and tetrazole forms depends on the electron density at the nitrogen atom common to the two rings. In this case the chemical nature of the substituents is of decisive importance. The presence of electron-donating substituents facilitates the closure of the condensed tetrazole ring and increases its stability by enhancement of the electron density at the common nitrogen atom. Electron-accepting substituents stabilise the azido-form:



The study of the azidoazomethine–tetrazole tautomerism has acquired practical importance.

Emulsion-photographic studies have been made[5,12,15,17,22] of tetrazolo[5,1-*b*]benzothiazoles, thiazolo[2,3-*e*]tetrazoles, and certain others. It has been shown that tetrazolo[5,1-*b*]benzothiazole and its derivatives are excellent stabilisers of silver chloride photographic emulsions.

It has been found that the stabilising effect of condensed tetrazoles depends on the state of the azidoazomethine–tetrazole equilibrium. Only those condensed tetrazoles which can give rise to azido-forms with an increased electron density at the heterocyclic nitrogen atom exhibit stabilising properties:



Thus tetrazolopyridine does not stabilise silver chloride emulsions, while 5-nitrotetrazolopyridine is an effective emulsion stabiliser. Infrared spectroscopy of these compounds showed that the former exists only in the tetrazole form in both the crystalline state and in solution. The latter exists in solution as an equilibrium mixture of the azido- and tetrazole forms. For this reason, alkyl

derivatives of thiazolo[2,3-*e*]tetrazole are not stabilisers, while 6-phenylthiazolo[2,3-*e*]tetrazole exhibits a fairly pronounced stabilising effect on the photographic emulsion.

II. METHODS FOR THE INVESTIGATION OF THE AZIDO-AZOMETHINE–TETRAZOLE TAUTOMERISM

The phenomenon of the azidoazomethine–tetrazole tautomerism has been studied in systems where the tetrazole ring is condensed with five- and six-membered aromatic nitrogen-containing heterocycles. The influence of the heterocycle and the electronic nature of its substituents, the polarity of the solvent, the pH of the medium, and temperature on the stability of the condensed tetrazole ring, its isomeric azido-derivative, or the state of the azidoazomethine–tetrazole equilibrium between them has been studied.

The possibility of the annelation of the tetrazole ring to thiazole[4,6,10-12,16,17,20-23,43], 1,2,4-triazole[44,45], thiadiazole[43], tetrazole[46], benzothiazole[1,2,4,6,9-12,14,16,17,19,21,22,24,27-29,47-51], benzoselenazole[27], benzoxazole[27], benzimidazole[26,52], naphtho[2,1-*d*]thiazole[53], naphtho[1,2-*d*]thiazole[53], pyridine[27,28,30,31,47,48,54-64], pyridazine[48,65-77], pyrimidine[27,33-35,47,48,63,69,70,78-87], pyrazine[48,67,79,88], 1,2,4-triazine[47,67,89,90], *s*-tetrazine[91,92], quinoline[93-96], isoquinoline[95], phthalazine[27,77,97,98], quinazoline[36,69-84,85,96,98-110], quinoxaline[96,97,101,111,112], 1,8-naphthyridine[113-122], pyrido[3,4-*d*]pyridazine[72,123,124], pyrido[2,3-*d*]pyridazine[123], 4*H*-pyridazino[6,1-*e*]-1,2,4-triazine[74,75], pyrazino[2,3-*d*]-pyridazine[125], phenanthridine[96,126,127], pyrrolo[1,2-*a*]quinoxaline[129], thieno[3,2-*d*]pyrimidine[129,130], imidazo[1,2-*o*]pyridazine[74,129,131], pyrazolo[1,5-*a*]pyrimidine[132,133], purine[134-137], *s*-triazolo[4,3-*b*]pyridazine[67,71,74,138,139], and *s*-triazolo[4,3-*b*]-*as*-triazine[67,140] has been examined in greatest detail.

The hypothesis of the occurrence of an equilibrium between the azido- and tetrazole forms was put forward on the basis of a study of the chemical properties of these compounds[2]. In certain cases the study of the chemical properties of condensed tetrazoles combined with infrared or NMR spectroscopy can be useful for a quantitative assessment of the equilibrium system. Thus Carboni and coworkers[114,116-118,120] established by a chemical method the proportions of the isomeric 8-azidotetrazolo[1,5-*a*]-1,8-naphthyridines in solutions. The method is based on the different chemical properties of the condensed tetrazole ring and the azido-group. In reduction reactions and in the interaction with nucleophilic agents the azido-group exhibits a higher reactivity. Consequently, in determining the structures and compositions of the products in the reaction mixtures, it is possible to estimate quantitatively the proportions of the isomers in solution.

It is sometimes possible to demonstrate the occurrence of the azidoazomethine–tetrazole equilibrium or even to separate the tautomers by paper and thin-layer chromatography.

In 1959 Boyer and Miller[28] used paper chromatography for the first time in the separation of tetrazolo[5,1-*b*]benzothiazole and 2-azidobenzothiazole and showed that the intensity of the luminescence in the ultraviolet of the two spots on the chromatogram depends on temperature, but no quantitative estimates were made for the equilibrium.

In order to study the azidoazomethine–tetrazole equilibrium and to separate the tautomers in the *s*-tetrazino[2,3-*e*]tetrazole-3-azido-*s*-tetrazine system, Ershov and Postovskii[91] used thin-layer chromatography on alumina.

A detailed study of the phenomenon of the azidoazomethine–tetrazole tautomerism and quantitative estimation of the composition of the equilibrium mixture became possible as a result of the wide-scale application of physical research techniques, primarily infrared and NMR spectroscopy.

The application of infrared spectroscopy is based on the fact that the azido-group has characteristic ν_{as} absorption bands in the range 2100–2200 cm^{-1} and ν_s bands in the range 1100–1350 cm^{-1}. The vibration bands of the tetrazole ring are more difficult to identify and they must be sought at 760, 1212, 1390, 1465, and 1480 cm^{-1}. By measuring the infrared spectra of the compounds in the crystalline state and in solution in polar and non-polar solvents, it is possible to detect the azido- or tetrazole forms of the compounds or both forms simultaneously. Similar measurements at elevated temperatures reveal a change in the intensities of the absorption bands of the azido-group and the tetrazole ring. The heat of the tetrazole–azide transformation can be determined from the temperature variation of the intensities of the absorption bands. It amounts to 4.65 and 0.98 kcal $mole^{-1}$ for the tetrazolo[5,1-*b*]benzothiazoles $\rightleftharpoons$ 2-azidobenzothiazole system in pyridine and dioxan respectively[29,51]. It has been shown that the transformation of the tetrazole into the azide is an endothermic process.

The application of NMR is based on the different effects of the azido-group and the tetrazole ring on the positions of the protons signal in the NMR spectra of the test compounds. These different effects are associated with the greater (in relation to the azido-group) electronegativity of the tetrazole ring. Therefore the proton signals referring to the tetrazole tautomer should occur in the region of lower fields compared with the proton signals due to the azido-tautomers. The nearest protons should be influenced most. The NMR spectra at elevated temperatures reveal an increase of the intensities of the signals of the protons belonging to the azido-form of the compound. This may be regarded as evidence for the validity of the assignment of the proton signals belonging to different tautomeric forms of the compounds.

Quantitative studies of the NMR spectra at different temperatures led to the calculation of the equilibrium constants for various tautomeric systems and to the determination of the heats of the tetrazole–azide transformations in different solutions[33,34,61,72,123,135,136]. These heats for tetrazolo[1,5-*a*]pyridine, tetrazolo[1,5-*a*]pyrimidine, tetrazolo[1,5-*a*]purine, and tetrazolo[5,1-*b*]purine are in the range 2.5–7.0 kcal $mole^{-1}$.

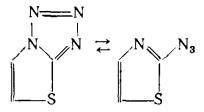
Until recently electronic spectroscopy was not used to investigate the azidoazomethine–tetrazole tautomerism, because the tetrazole ring does not absorb in the ultraviolet and the azido-group gives rise to low-intensity bands at 280 nm. Ershov and Postovskii[91] were the first to employ the ultraviolet spectra to investigate the influence of solvent polarity and to examine the time variation of the tautomeric equilibrium in the *s*-tetrazino[2,3-*e*]tetrazole $\rightleftharpoons$ 3-azido-*s*-tetrazine system. This became possible because the authors separated the tautomers and isolated one of them in a pure form.

III. INFLUENCE OF THE NATURE OF THE NITROGEN-CONTAINING HETEROCYCLE ON THE STABILITY OF CONDENSED TETRAZOLES

The stability of the condensed tetrazole ring is to a large extent determined by the nature of the nitrogen-containing heterocycle to which it is annelated. The

tetrazole ring condensed with saturated heterocycles (trimethylene-[28], tetramethylene-[141,142], and pentamethylene-tetrazoles[142,143], as well as other derivatives[141,144-147], and the nitrogen analogue of trimethylenetetrazole-tetrazoloimidazolidine[28,141]) do not differ in their stability from the 1,5-disubstituted tetrazoles. In the crystalline state and in solution they have cyclic structures.

However, the condensation of the tetrazole ring with a five-membered aromatic heterocycle (thiazole, triazole, tetrazole) leads to a sharp decrease of the stability of the former. The nature and number of heteroatoms in the five-membered heterocycle influence appreciably the stability of the tetrazole ring. Thus in the crystalline state the equilibrium in system (I)

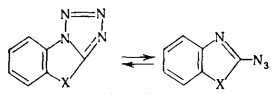


(I)

is almost completely displaced towards thiazolo[2,3-*e*]-tetrazole. However, the tetrazole ring in the latter compound is relatively unstable and tends to be converted into the isomeric azido-form even on dissolution.[20]

It has also been reported that the pyrazole[27], triazole[44], thiadiazole[43], and tetrazole[46] rings destabilise the tetrazole ring condensed to them. For example, 5-azidotetrazole and 5-aryl-3-azido-1,2,4-triazole do not undergo ring closure to the corresponding tetrazoles.

It has been shown[10,11] that tetrazolo[5,1-*b*]benzothiazole (II) is more stable than thiazolo[2,3-*e*]tetrazole (I), as can be seen from the effect of the same solvents on these compounds (see below):

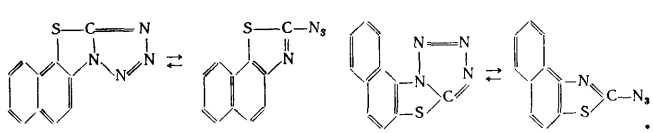


(II-VI)

where X = S (II), Se (III), O (IV), NH (V), and SO_2 (VI).

In systems (II)-(VI) the states of the azidoazomethine-tetrazole equilibrium and the stability of a particular isomeric form depends to a large extent on the electronegativity of the atom X[27]. When X = S or Se, compounds (II) and (III) have the structures of condensed tetrazoles, although they are much less stable than the 1,5-disubstituted tetrazole and exist in solution in equilibrium with the isomeric azido-forms[10,11,16,17,20,27-29]. The replacement of the sulphur atom in the tetrazole (II) by the sulphone group (VI) leads to an increase of the stability of the azido-form and precludes its ring closure[27]. The attempts to obtain tetrazole rings condensed with benzoxazole or benzimidazole rings also did not lead to the desired results. The compounds synthesised had the structures of 2-azido-derivatives of benzoxazole (IV) and benzimidazole (V).

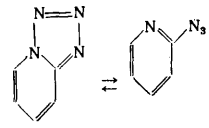
The condensation of the thiazole ring in (I) with the naphthalene ring [systems (VII) and (VIII)] reduces the stability of the corresponding tetrazole forms relative to tetrazolo-[5,1-*b*]benzothiazole (II):



(VII) (VIII)

Even in the crystalline state tetrazolo[1,5-*b*]naphtho-[1',2'-*d*]thiazole (VII) and tetrazolo[1,5-*b*]naphtho[2',1'-*d*]thiazole (VIII) exist in equilibrium with the isomeric azido-derivatives and in the latter case the equilibrium is displaced towards the azido-form. The authors attribute this decrease of stability to the fact that naphthothiazoles have more pronounced electron-accepting properties than benzothiazoles[53].

In the crystalline state tetrazolo[5,1-*a*]pyridine (IX) has a cyclic structure and is not converted into the isomeric azido-derivative in polar and non-polar solvents[27,61,48,63]:

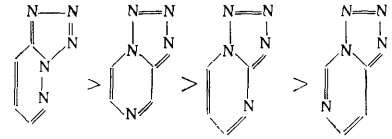


(IX)

However, under severe conditions (in pyrolysis) it can give rise to the reactive azido-form and can enter into reactions characteristic of azides[62,63,47,147].

It follows from a series of studies by Temple and coworkers[33-35], Wentrup[48,70,82], Stanovnik[74,75], and others[65,88] that the replacement of the methine group in the six-membered nitrogen-containing heterocycle by a second electronegative atom (nitrogen) causes some decrease of the stability of the $N_{(1)}-N_{(2)}$ bond in the condensed tetrazole ring. In the crystalline state tetrazolo[1,5-*b*]pyridazine (X)[48,65], tetrazolo[1,5-*a*]pyrazine (XI)[48,70,88], and tetrazolo[1,5-*a*]pyrimidine (XII)[33-35,48] have cyclic structures. Tetrazolo[1,5-*c*]pyrimidine (XII) is in equilibrium with the isomeric 4-azidopyrimidine even in the crystalline state[35]. In polar and non-polar solvents compounds (X)-(XIV) exist in both tautomeric forms, but on heating they behave like azides.

Thus the state of the azidoazomethine-tetrazole equilibrium involving the above heterocycles depends on the relative positions of the two nitrogen atoms in the heterocycle and in compounds (XII) and (XIII) also on the bond of the pyrimidine ring to which the tetrazole ring is attached. These compounds can be arranged in the following sequence in terms of the stability of the condensed tetrazole ring:



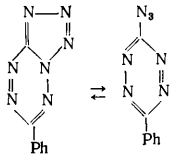
(X) (XI) (XII) (XIII)

This relation is manifested particularly clearly when the influence of temperature and solvent on the state of the azidoazomethine-tetrazole equilibrium is examined.

An increase in the number of nitrogen heteroatoms in the six-membered ring leads to a further destabilisation of the tetrazole ring condensed to it and to an increase of the stability of the azido-form. Ershov and Postovskii[91] carried out calculations for the azido-forms of a number of phenylazines and showed that, with increase of the number of nitrogen atoms in the ring, the π-electron density at the bridgehead nitrogen atom diminishes, which leads to an increase of the energy of the transition to the tetrazole form and to an increase of the stability of the azido-form.

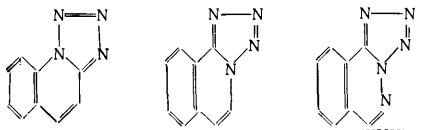
Unsubstituted azidotriazines and azidotetrazines or their isomeric condensed tetrazoles have not been described in the literature. The structures of their derivatives depend on the electronic nature of the substituents and confirm indirectly the calculations of Ershov and Postovskii[91].

Ershov and Postovskii showed that 6-phenyltetrazolo-[5,1-*b*]-*s*-tetrazine (XIV) cannot be isolated in a pure state because of the exceptional ease of its conversion into the azido-form owing to the latter's greater stability[91]:



(XIV)

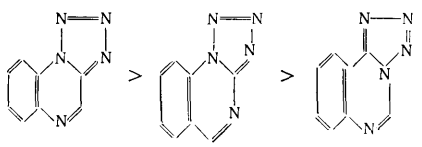
The benzo-analogues of compounds (IX)–(XIII) and (XV)–(XX) contain more stable tetrazole rings. Thus tetrazolo-[1,5-*c*]quinoline (XV) and its analogue tetrazolo[5,1-*a*]isoquinoline (XVI) exist only in the cyclic form[95].



(XV) (XVI) (XVII)

Under severe conditions (380–510°C/10^{-3}–10^{-2} mmHg), they isomerise, like compound (IX), to the corresponding azides. The existence of tetrazolo[1,5-*a*]phthalazine (XVII), but not of its isomeric 1-azidophthalazine, has been reported[27,77,97,98]. Tetrazolo[1,5-*e*]quinazoline (XX) is more stable than the related tetrazolo[1,5-*c*]pyrimidine (XIII). Thus in the crystalline state compound (XX) exists only in the cyclic form[103] and compound (XIII) is present in equilibrium with the azide[35]. Tetrazolo[1,5-*a*]quinoxaline (XVIII) is more stable than tetrazolo[1,5-*a*]pyrazine (XI). This is confirmed by the cyclic structure of compound (XVIII) even in trifluoroacetic acid, in contrast to compound (XI).[101]

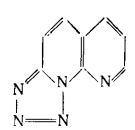
Compounds (XVIII)–(XX) can be arranged in the following sequence in terms of the stability of the condensed tetrazole ring:



(XVIII) (XIX) (XX)

which is analogous to the series (XI) > (XII) > (XIII) discussed above. Thus, in contrast to compound (XVIII), the tetrazoloquinazolines (XIX) and (XX) are converted into the corresponding azides in trifluoroacetic acid[69,101]. The greater stability of tetrazolo[1,5-*a*]quinazolines (XIX) compared with tetrazolo[1,5-*c*]quinazolines (XX) is confirmed by the gradual transformation, observed by Postovskii and coworkers, of certain derivatives of (XX) into the isomeric azido-derivatives in the crystalline state[100,109], which is not observed for compounds of type (XIX).[36]

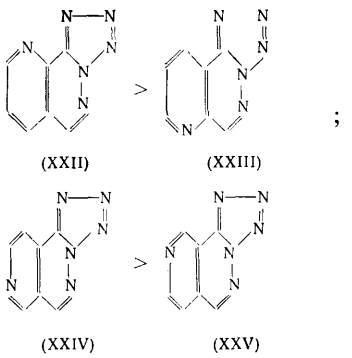
The replacement of the benzene ring in the condensed tetrazoles (XV) and (XVII) by pyridine leads to the somewhat less stable tetrazolo[1,5-*a*]-1,8-naphthyridine (XXI)[114,122]:



(XXI)

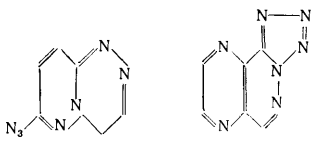
and also to the pyridotetrazolopyridazines (XXII)–(XXV)[72,73,123,124]. The stability of the tetrazoles (XXII)–(XXV) depends on the position of the nitrogen atom in the pyridine ring relative to the condensed tetrazole ring.

This can be inferred indirectly from the ability of 6-azidopyrido[3,2-*d*]tetrazolo[5,1-*b*]pyridazine and 6-azidopyrido[3,4-*d*]tetrazolo[1,5-*b*]pyridazine to isomerise to the thermodynamically more stable 6-azidopyrido[2,3-*d*]-tetrazolo[5,1-*b*]pyridazine and 6-azidopyrido[4,3-*d*]tetrazolo[1,5-*b*]pyridazine respectively[72,123,124]. It follows from these data that compound (XXII) is more stable than compound (XXIII) and compound (XXIV) is more stable than compound (XXV):



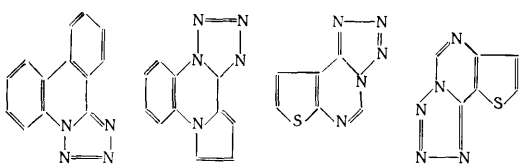
(XXII) (XXIII) (XXIV) (XXV)

It has been shown in a series of studies by Stanovnik and Tisler[74,75] that the condensation of the pyridazine ring to heterocycles containing two nitrogen atoms leads to the formation of the azido-derivative (XXVI) instead of the isomeric condensed tetrazoles. On the other hand, compound (XXVII) exists in the cyclic form:



(XXVI) (XXVII)

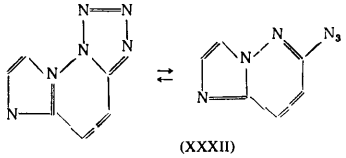
It has been reported[96,126,127] that the condensation of the 9,10-phenanthridine ring with the tetrazole ring leads to the stable tetrazolo[1,5-*b*]-9,10-phenanthridine (XXVIII). Pyrrolo[1,2-*a*]tetrazolo[1,5-*c*]quinoxaline (XXIX) has also been described[87]:



(XXVIII) (XXIX) (XXX) (XXXI)

The systems (XXX) and (XXXI), derived from tetrazolo[1,5-*c*]pyrimidine (XIII) in which the pyrimidine ring is in its turn condensed to a five-membered ring (thiophen) have been described[128,130]. The substances are said to have a cyclic structure in the crystalline state.

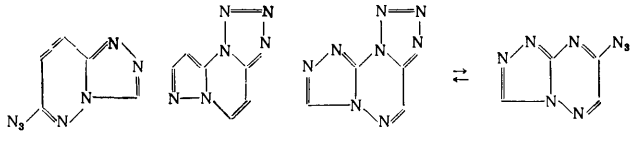
The condensation of tetrazolo[1,5-*c*]pyridazine (X) with a five-membered nitrogen-containing ring (imidazole) leads to the destabilisation of the tetrazole ring in imidazo[1,2-*b*]tetrazolo[5,1-*f*]pyridazine (XXXII):



(XXXII)

It has been stated that even in the crystalline state compound (XXXII) exists in equilibrium with a small amount of the isomeric azido-form[131]. The accumulation of nitrogen atoms in the five-membered ring precludes the closure of the tetrazole ring. 6-Azido-*s*-triazolo[4,3-*b*]-pyridazine (XXXIII), which does not isomerise to the corresponding tetrazole, has been described[67,71,74,138,139].

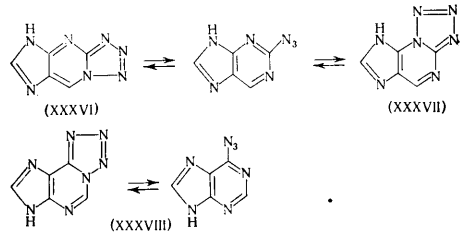
On the other hand, the condensation of tetrazolo[1,5-*c*]-pyrimidine (XIII), which is less stable than compound (X), with the pyrazole ring leads to the formation of the stable pyrazolo[1,5-*a*]tetrazolo[1,5-*c*]pyrimidine (XXXIV), which has only the cyclic structure in the crystalline state[132]:



(XXXIII) (XXXIV) (XXXV)

In the crystalline state the equilibrium in system (XXXV) is fully displaced towards the cyclic form, while in solution there is an equilibrium between both tautomers[67,140].

The condensation of the pyrimidine ring in the tetrazolopyrimidines (XII) and (XIII) with the imidazole ring leads to the formation of the tetrazolopurines (XXXVI), (XXXVII), and (XXXVIII) in which the stability of the tetrazole ring is sharply reduced compared with the related tetrazolopyrimidines:



(XXXVI) (XXXVII)

(XXXVIII)

The studies of Temple and coworkers[134-136] have shown that tetrazolo[5,1-*a*]purine (XXXVIII) exists in the crystalline state in equilibrium with 6-azidopurine, while in the system (XXXVI)–(XXXVII) the equilibrium is almost completely displaced towards 2-azidopurine. However, under certain conditions the azido- and two tetrazole forms can be in equilibrium. These compounds can be arranged in the following sequence in terms of the stability of the tetrazole ring: (XXXVIII) > (XXXVI) > (XXXVII).

IV. INFLUENCE OF SUBSTITUENTS

The electronic nature of the substituent in the nitrogen-containing heterocycle has a considerable influence on the possibility of the formation of the condensed tetrazole ring and its stability and also on the state of the azidoazomethine–tetrazole equilibrium in the system. As a rule, the introduction of powerful electron-donating substituents, which increase the electron density at the nitrogen heteroatom, promotes the formation of condensed tetrazoles in chemical reactions, increases the stability of the condensed tetrazole ring, and shifts the azidoazomethine–tetrazole equilibrium towards the cyclic form. The introduction of powerful electron-accepting substituents, which reduce the electron density at the nitrogen heteroatom, leads to an appreciable decrease of the stability of the condensed tetrazole ring and to a shift of the equilibrium in the tetrazole ⇌ azide system towards the azido-tautomer. A powerful electron acceptor introduced into the nitrogen-containing heterocycle sometimes precludes altogether ring closure by the azido-group via the nitrogen atom and the formation of a condensed tetrazole ring is not observed.

In systems containing a tetrazole ring condensed with five-membered nitrogen-containing heterocycles this phenomenon has been studied in greatest detail for thiazolo[2,3-*e*]tetrazoles (I) and tetrazolo[5,1-*b*]benzothiazoles (II). Thus Pochinok and coworkers[10,14,16,20,23,24] studied the influence of substituents on the possibility of the annelation of the tetrazole ring to the thiazole and benzothiazole rings and the state of equilibrium in systems (I) and (II). It has been shown that electron-donating substituents in the thiazole and benzathiazole rings facilitate the closure of the condensed tetrazole ring and increase its stability. Thus thiazolo[2,3-*e*]tetrazole (I) and its 5-methyl, 6-methyl, 5,6-dimethyl, 6-phenyl, 6-*p*-tolyl, 6-*p*-bromophenyl, 6-*p*-chlorophenyl, 5-bromo-6-methyl, and 6-thiacyanato-derivatives are condensed tetrazoles in the crystalline state. The introduction of the electron-accepting nitro-, sulpho-, chlorosulphonyl, aminosulphonyl, thiacyanato-, or bromo-groups in the 5-position of 6-phenylthiazolo[2,3-*e*]tetrazole (I) decreases appreciably the electron density at the nitrogen atom of the thiazole ring and therefore ring closure by the azido-group via this atom becomes impossible; such derivatives of (I) exist in the azido-form even in the crystalline state. When substituents such as methyl and the bromo-group, methyl and the thiacyanato-group, or the bromo- and thiacyanato-groups are combined in a derivative of (I), the stability of the tetrazole ring also diminishes. However, the presence of the electropositive methyl group in such molecules imparts a certain stability to the tetrazole forms of these compounds in the crystalline state, although in solution (in chloroform, carbon tetrachloride, and acetonitrile) the equilibrium in these systems is almost completely displaced towards the isomeric azides.

Similar relations are observed in systems (II). Tetrazolo[5,1-*b*]benzothiazole and its 6-methyl, 8-methyl, 6-methoxy-, 8-methoxy-, 6-acetamido-, 6-chloro-, 6-bromo-, and 6-fluoro-derivatives are condensed tetrazoles in the crystalline state. The introduction of chlorine in the 4-position of the benzothiazole ring leads to the formation of the isomeric 2-azido-4-chlorobenzothiazole instead of the tetrazole, which is a consequence of the greater influence of the negative inductive effect of the chlorine in the 4-position of the benzothiazole ring compared with the chlorine in the 6-position. The chlorine atom in the 4-position does not give rise to steric hindrance, which might interfere with the formation of the condensed tetrazole, while the analogous compound with the CH_3 group in the 4-position has the cyclic structure.

The introduction of an electron-accepting substituent (the nitro-group) in the 4-, 5-, 6-, and 7-positions of the

benzothiazole ring leads to the existence of stable 2-azido-derivatives even in the crystalline state.

6-Carboxy-derivatives of (II) exist in equilibrium with the azido-form even in the crystalline state, which can be accounted for by the approximately identical electron-accepting properties of the carboxy-group and the tetrazole ring[148,149]. The formation of salts via the carboxy-group results in a decrease of the electron-accepting properties of the substituent and therefore the sodium salt exists as the tetrazole tautomer in the crystalline state.

Boyer and coworkers[28,30] showed that the introduction of hydroxy- and amino-groups into tetrazolo[5,1-*a*]pyridine (IX) does not destabilise the tetrazole ring and the resulting 6- and 8-hydroxy- and 8-amino-derivatives of (IX) have a cyclic structure in both the crystalline state and in solutions (in dimethylformamide, alcohol, and chloroform). The introduction of the electron-accepting nitro-group into the 6-position of compound (IX) reduces the stability of the condensed tetrazole ring, which leads to the formation under certain conditions of an equilibrium system containing both tautomers[28,65,88]. The chlorine atom introduced into the α-position of the pyridine ring acts similarly[61,95]. It has been found that the introduction of chlorine in the 5-position of compound (IX) destabilises the tetrazole form and shifts the equilibrium towards the azide.

It has also been reported[115,117-120,122] that tetrazolo[1,5-*a*]-1,8-naphthyridines (XXI) with electron-donating substituents have only the cyclic structure in the crystalline state with the exception of 8-hydroxy-5-phenyltetrazolo[1,5-*a*]-1,8-naphthyridine[74], which is an azide in the crystalline state. The phenyl substituent decreases the stability of the condensed tetrazole ring in compound (XXI) when it is in the 5-position, evidently because it attracts electrons to itself. This can explain the presence of the $\nu_{as}(N_3)$ band in the infrared spectrum of 8-hydroxy-5-phenyltetrazolo[1,5-*a*]-1,8-naphthyridine in the crystalline state[117] (although under certain conditions the pure tetrazole form can be isolated). On the other hand, when the phenyl substituent is in the 4-position, it stabilises the condensed tetrazole ring as a result of conjugation with the latter.

Similar features were observed in the series of substituted tetrazolo[1,5-*a*]pyrimidines (XII)[33,34,48]. The introduction of two methyl groups, a methyl and a methoxy-group, or a methyl and a methylthio-group into the pyrimidine ring stabilises the condensed tetrazole ring in such systems in relation to the unsubstituted compound (XII).

The introduction of chlorine, which exhibits a stronger negative inductive effect, as a substituent in the 5-position leads to an appreciable destabilisation of the ring compared with the unsubstituted compound (XII). The chloro-derivative of (XII) can be isolated in a pure state when solutions in $CHCl_3$ or CF_3COOH are evaporated and remains metastable for several weeks. However, after prolonged storage it is gradually converted into the more stable tetrazole form. The same process takes place rapidly when compound (XII) is heated above its melting point. Thus both isomers were isolated for the first time in a pure form.

The introduction of the electron-donating amino-group or the methyl group, which exhibits a powerful positive inductive effect, in the 8-position of tetrazolo[1,5-*c*]pyrimidine (XIII) stabilises the tetrazole ring. Thus 5,7,8-trimethyltetrazolo[1,5-*c*]pyrimidine is more stable than the 5,7-dimethyl derivative[14]. 8-Amino-7-chlorotetrazolo-[1,5-*c*]pyrimidine exists in the crystalline state as the tetrazole form. Acylation of the amino-group in the 8-position (with acetic or trifluoroacetic acid) or the introduction of the ethoxymethyleneamino-group in the 8-position leads to the occurrence of the tetrazole $\rightleftharpoons$ azide equilibrium even in the crystalline state, the equilibrium being displaced towards the azido-tautomers[35,86]. When the electron-donating substituent is in the 7-position, its influence on the stability of the tetrazole rings may be various. Thus Postovskii and Smirnova[87] investigated the influence of cycloalkylamino-residues in the pyridine ring on the state of the tetrazole $\rightleftharpoons$ azide equilibrium in system (XIII). It was found that the electron-donating cycloalkylamino-substituents with related structures have different effects on the stabilities of these compounds. When the ring contains morpholine and homopiperidine residues, the compounds exist in the form of azides even in the crystalline state. The pyrrolidino- and piperidino-derivatives are tetrazoles in the crystalline state. This difference between the structures cannot be related to the different basicities of the substituents, since the basicities of homopiperidine, pyrrolidine, and piperidine are approximately of the same order of magnitude. The authors suggested that the observed differences are probably due to the steric effect of the substituents.

It has also been reported[48] that the introduction of two-methoxy-groups into tetrazolo[1,5-*c*]pyrimidine (XIII) in the 5- and 7-positions precludes the formation of the condensed tetrazole ring, which cannot be accounted for by steric hindrance.

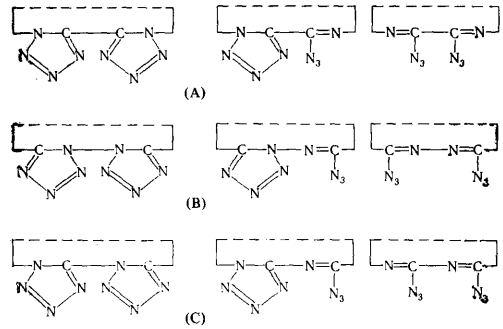
The introduction of the methyl, phenyl, γ-pyridyl, or α-furyl substituents in the 5-position of tetrazolo[1,5-*c*]-quinazoline (XX) does not destabilise the tetrazole form. These compounds have only the cyclic structure in both the crystalline state and in solutions[109]. The introduction of cycloalkylamino-residues into the 5-position of (XX) destabilises the cyclic form and makes possible its conversion into the isomeric azido-form even in the crystalline state after prolonged storage followed by the determination of the azideazomethine–tetrazole equilibrium position[36]. The rate of conversion of the tetrazole into the azide then depends on the basicity of the cycloalkylamino-residue. In contrast to compound (XX), tetrazolo-[1,5-*a*]quinazoline (XIX) with cycloalkylamino-groups in the 5-position has the cyclic structure in the crystalline state[99]. It has been shown[67] that the introduction of two phenyl groups in the 5- and 6-positions of tetrazolo[1,5-*a*]-pyrazine (XI) also leads to the destabilisation of the tetrazole ring.

The introduction of chloro- and methoxy-groups[25] in the 5-positions and cycloalkylamino-groups in the 6-position[68] of tetrazolo[1,5-*b*]pyridazine (X) does not evidently reduce the stability of the condensed tetrazole ring. The authors attribute the appearance of weak bands in the infrared spectrum of cycloalkylaminotetrazolo[1,5-*b*]pyridazine in the range 2100–2200 cm^{-1} to overtones or combination tones of the fundamental vibrations of the heterocycle in the region of the asymmetric vibrations of the azido-group[68].

Temple showed[36] that in purine systems the structure of azidotetrazole derivatives also depends on the presence of electron-donating or electron-accepting substituents. Thus 2-azidopurine exists almost completely in the form of the azide in the crystalline state. The introduction of the electron-donating hydroxy-group in the 6-position of 2-azidopurine leads to the appearance of one of the cyclic forms, which is completely converted into 2-azidopurine after only 30 min even after dissolution in trifluoroacetic acid (TFA)[136]. The amino-group has a similar effect, but in this case the two possible tautomers appear in d_6-DMSO. On the other hand, chlorine in the 2-position of 6-azidopurine appreciably stabilises the azido-form.

In the crystalline state and in solution in dimethyl sulphoxide (DMSO) the compound (XXVII) exists in the form of the azide, in contrast to unsubstituted 6-azidopurine.

Attempts have been made to synthesise compounds containing two condensed tetrazole rings in a single molecule or to condense two such rings with one nitrogen-containing heterocycle in a system of type (A)–(C):

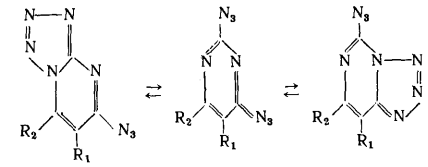


Behringer and Fischer[150] studied non-condensed linear systems of types (A) and (B) and showed that in type (A) systems there is isomerisation to the more stable bistetrazole with the same charge distribution on the nitrogen atoms of the two rings as in the unsubstituted tetrazole. Bistetrazoles of type (B) are as a rule extremely unstable and exist in the form of the isomeric diazides[150,151]. However, it proved possible to isolate 1,1-bis-(5-phenyl)-tetrazole in the crystalline state[150], while in solution the compound is in equilibrium with the isomeric diazide.

Not one case where two tetrazole rings are present in the molecule simultaneously has been described for condensed systems. The attempts to condense the tetrazole ring with another tetrazole ring[46] or two tetrazole rings with pyridazine[65,67,72], pyrimidine[27,48,152–154], tetrazine[92], phthalazine[27,98], quinazoline[72,123], quinoxaline[27,98,103], pyrido[3,2-*d*]pyridazine[72,123], pyrido[4,3-*d*]pyridazine[123], naphthyridine[113,114,117–121], pyrazino[2,3-*c*]pyridazine[125], and purine[136,137] did not lead to the desired results. The reason for this is probably the powerful electron-accepting properties of the tetrazole rings and the consequent decrease of the basicity of the second nitrogen heteroatom. The second azido-group can play the role of a weak electron-donating substituent in such cases.

In most instances compounds of this kind exist as azidotetrazoles in the crystalline state. Azidoazomethine ⇌ tetrazole equilibrium systems arise in solutions and their tautomer content depend on the nature of the heterocycle and the substituents and also on the polarity of the solvent. Sometimes transitions of this kind occur after prolonged storage or heating of the compound.

Thus the structure of diazides was attributed in a number of studies[27,152–154] to 2,4-diazidopyrimidine and its derivatives (6-methyl, 5-methyl, 5,6-dimethyl, 6-phenyl, and 6-furyl) on the basis of an investigation of certain physical and chemical properties. Later studies by Wentrup[48] by NMR showed that at any rate methyl and dimethyl derivatives exist in the crystalline state as tautomeric mixtures of azidotetrazoles (XII, a-c) and (XIII, a-c) in which the more stable (XII, a-c) predominates.

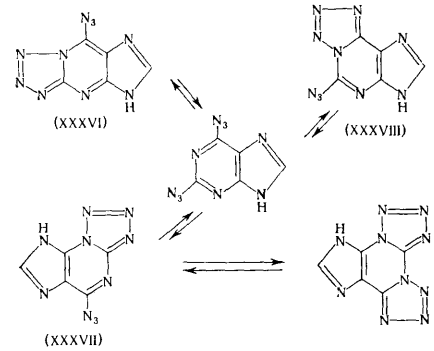


(XII) (XIII)

(a) R_1 = Me, R_2 = H; (b) R_1 = H, R_2 = Me; (c) R_1 = R_2 = Me.

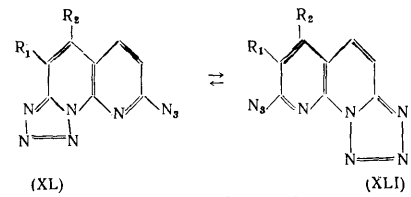
The diazido-forms of the methyl derivatives can be isolated in a pure state only under special conditions; they are metastable at room temperature. At the melting point such diazides are converted into a mixture of the isomeric tetrazoles (XII) and (XIII) which on further heating reforms the diazide. In chloroform solution all three isomers are in tautomeric equilibrium.

Smirnova and Postovskii[137] and Temple et al.[136] showed that, out of the five possible isomeric compounds in the 2,6-diazidopurine system, it is possible to detect 2,6-diazidipurine itself in the crystalline state (and in trifluoroacetic and acetic acids), while in DMSO solution two azidotetrazoles, probably (XXXVI) and (XXXVIII), can be detected in addition to the diazide.



(XXXVI) (XXXVIII) (XXXVII)

The introduction of substituents into the naphthyridine ring of azidotetrazolonaphthyridine leads to the formation of a series of isomeric substituted azidotetrazolonaphthyridines:



(XL) (XLI)

(a) R_1=Me, R_2=H
(b) R_1=H, R_2=Me
(c) R_1=Ph, R_2=H
(d) R_1=H, R_2=Ph

On the basis of a study of chemical properties and infrared spectra, Carboni and coworkers showed that such substances exist in the crystalline state in the form of only one tautomer whose structure was not established. On dissolution, the tautomeric equilibrium (XL) ⇌ (XLI, a-d) arises and the isomer content in such equilibrium is determined by the position of the substituent in the naphthyridine ring relative to the condensed tetrazole ring. When R_1 = Me or Ph, the tetrazole ring is stabilised as a result of conjugation and the isomers (XL, a and c) predominate in the system. When R_2 = Me or Ph, the tetrazole ring condensed with the unsubstituted ring is more stable and the isomers (XLI, b and d) predominate. In the crystalline

state these compounds probably have the structures (XL, a and c) and (XLI, b and d) respectively. Evidence is presented to show that the molecular ions derived from some of these compounds have the ditetrazole structure. Thus pyrolysis of 6-azidotetrazolo[1,5-*b*]pyridazines and 6-azidopyridotetrazolo[1,5-*b*]pyridazines results in the liberation of six nitrogen atoms, which indicates the existence of an intermediate ditetrazole structure[155].

V. INFLUENCE OF SOLVENTS AND TEMPERATURE

The state of the azidoazomethine–tetrazole equilibrium in solutions has been studied in most systems (I, II, VII–XIV, XIX–XXI, XXXVI, XXXVII) using various polar and non-polar solvents: DMSO, d_6-DMSO[33–35,48,61,67,72,86,123,135,136], pyridine[29,33–35,51,87,91,120], acetone, deuterioacetone[33–35,61], dioxan[29,51,87], methanol, deuteriomethanol[33,34,56], dimethylformamide[33,34,67,91,120,131], tetrahydrofuran[67], chloroform, deuteriochloroform[10,16,17,20,29,34,48,51,65,67,68,70,87], carbon tetrachloride[10,16,17,20,29,51,53,87], benzene[29,51,87,91], n-heptane[91], H_2O[70], D_2O[135], NaOD solution[135], acetic acid[114,135,136], TFA[33–35,48,61,65,67,69,101,117,120,135,136], $HF.SbF_5$,[48] and SO_2.[48]

In comparing the action of solvents on various condensed tetrazoles account must be taken in the first place of the stability of the system itself. However, apart from the nature of the annelated nitrogen-containing ring and the electronic structure of its substituents, in solution the stability of the condensed tetrazole ring and of the isomeric azido-derivative or the state of equilibrium between them is in addition greatly influenced by the polarity of the solvent. The dissolution of condensed tetrazoles is frequently but by no means always accompanied by ring opening. On the other hand, a polar solvent sometimes increases the stability of the condensed tetrazole or even promotes the cyclisation of the azide. The constants K_T for the same systems in different solvents are quoted in a review[42]. These data show that a decrease in solvent polarity destabilises the cyclic form and promotes its partial or complete isomerisation to the azide form. When the solvent interacts with the condensed system, for example protonates the second nitrogen atom in tetrazolopolyazines, the azide form is produced.

It has been shown[14,17] that, on dissolution of tetrazolo[5,1-*b*]benzothiazole (II) in concentrated sulphuric acid, TFA, or dimethyl sulphate, the isomeric azido-form is not produced. It is interesting that 2-azido-4-chlorobenzothiazole is converted in the same solvents into the isomeric 8-chlorotetrazolo[5,1-*b*]benzothiazole. In acids this process is accompanied by the protonation of the condensed tetrazole ring and the formation of a tetrazolium salt. With decrease of solvent polarity, compound (II) and its derivatives with electron-donating substituents are partly (in pyridine, acetonitrile, dioxan, and chloroform) or fully (in carbon tetrachloride) converted into the azido-form. The state of tautomeric equilibrium in system (II) depends on the stability of the ring, which is determined by the electronic influence of the substituent and the polarity of the solvent. Thus compound (II) and its derivatives with methyl and methoxy-groups are in equilibrium with the azido-form in acetonitrile, dioxan, pyridine, and chloroform, while in carbon tetrachloride the equilibrium is fully displaced towards the azido-tautomer. The introduction of halogen atoms (F, Cl or Br) into the benzothiazole ring leads to the destabilisation of the tetrazole ring and the consequent full isomerisation to the azide even in acetonitrile[17]. Similar features are observed in the series of thiazolo[2,3-*e*]tetrazoles.

Tetrazolo[5,1-*a*]pyridine (IX) is converted in solutions into the isomeric 2-azidopyridine. However, the introduction in the 6-position of the nitro-group, which destabilises the cyclic system, affects the behaviour of the latter on dissolution. In chloroform, deuteriochloroform, trifluoroacetic acid, and acetone an equilibrium is established between the isomeric azido- and tetrazole forms[28,61,65,88].

The tetrazoloazines (X)–(XIII), which are less stable than compound (IX), exist in solution in polar and non-polar solvents in equilibrium with azides and with decrease of solvent polarity the equilibrium is displaced towards the azido-form. Compound (X), which is the most stable in this series, exists in polar solvents almost completely in the cyclic form[48].

The equilibrium tetrazolo[1,5-*a*]pyrimidine ⇌ 2-azidopyrimidine (XII) is displaced in d_6-DMSO towards the tetrazole tautomer (K_T = 0.07) and with decrease of solvent polarity the content of the azido-form increases with a corresponding increase of the tautomeric equilibrium constant K_T, which is 0.37 in d_6-acetone. In chloroform, which is still less polar, only the azido-form (XII) exists[48].

Owing to the influence of the methyl groups, the stability of the condensed tetrazole ring in the 5,7-dimethyl derivative (XII) is somewhat greater. Therefore only the tetrazole form exists in d_6-DMSO[33,34,48]. With decrease of solvent polarity, there is a similar shift of the equilibrium towards the azide and an increase of K_T, which is 0.12 in d_6-methanol, 0.14 in pyridine, and 0.36 in deuteriochloroform[33,34]. The last value of K_T corresponds to the ratio tetrazole:azide = 1 : 3.[48] When a 6.8% chloroform solution of compound (XII) is diluted to 5.4% with the polar d_6-DMSO, K_T diminishes from 0.36 to 0.1 owing to the increase of the content of the tetrazole form in the system[33,34]. A similar influence of the solvent has been observed also for other substituted tetrazolo[1,5-*a*]pyrimidines[48].

It has also been shown[35,48] that in the tetrazolo[1,5-*c*]-pyrimidine ⇌ 4-azidopyrimidine (XIII) system with electron donating substituents in the pyrimidine ring the tetrazole ring is destabilised to a greater extent in the less polar d_6-acetone, pyridine and deuteriochloroform than in d_6-DMSO. For example, the ratio of the azide form (XIII) and the tetrazole form of the 7-methyl-5-methylthio-derivative is 1 : 16 in deuteriodimethyl sulphoxide and 5 : 1 in deuteriochloroform[48].

Postovskii and coworkers showed that in solutions in alcohol, dimethylformamide (DMF), and benzene 6-phenyltetrazolo[5,1-*c*]tetrazine (XIV) is in equilibrium with the azido-form (4 : 1, 1 : 1 and 2 : 3 respectively).[91] It has also been shown[47,67,90] that, on dissolution in chloroform, tetrahydrofuran, and trifluoroacetic acid, 5,6-diphenyltetrazolo[1,5-*c*]-1,2,4-triazine is in equilibrium with the azido-tautomer.

Temple's studies have shown that, on dissolving 2-azidopurine in d_6-DMSO, a system is produced in which the azido-tautomer is in equilibrium with two tetrazolopurines, (XXXVI) and (XXXVIII), in proportions of 3 : 6 : 1 respectively[94]. Similarly the dissolution of 6-amino-2-azidopurine in DMSO results in a system with the azido-form and the tautomers (XXXVI) and (XXXVIII) in proportions of 1 : 9.5 : 2.

In TFA the majority of tetrazoloazines exist in the azido-form or the latter predominates in the tautomer mixture, despite the fact that TFA can be classified as a polar solvent. This is probably a result of the protonation of the nitrogen atom of the heterocyclic base condensed

with the tetrazole ring or sometimes possibly of the substituent capable of being protonated. The positive charge is delocalised over the entire heterocycle and the electron-donating capacity of the latter, which favours the existence of the tetrazole form, diminishes.

Postovskii and coworkers[27] established that the hydrochloride and picrate of 7-piperidinotetrazolo[1,5-*c*]pyrimidine exist virtually as the azide in the crystalline state, while the base is in the tetrazole form. This example rules out the influence of solvation in this instance on the state of the azideazomethine–tetrazole equilibrium and apparently indicates an effect of protonation.

The studies of Postovskii and coworkers[29,51], Temple and coworkers[33-35,135], Sasaki et al.,[61] and Stanovnik and coworkers[72,123] showed that the transformation of the tetrazole form into the azido-form is an endothermic process and its heat is in the range 1–7 kcal mole^{-1}, a slight increase of temperature displacing the equilibrium towards the azido-form. This is indicated by the increase of the equilibrium constant, the increase of the intensity of the azide band observed in the infrared spectrum, and the decrease of that of the tetrazole bands. Similar features are shown also by the NMR spectra. The study of the pyrolysis of condensed tetrazoles in the gas phase by mass spectroscopy revealed that the first stage in the pyrolytic process is the tautomeric transformation of the tetrazole into the azide[48]. The opening of the tetrazole ring to form the azide with increase of temperature and ring closure to convert the azide into the tetrazole on reducing the temperature to the previous value can occur in both the crystalline state and in solution. The most stable tetrazolo[1,5-*a*]pyridine (IX) and tetrazolo[1,5-*b*]-pyridazine (X) do not isomerise to the corresponding azides on raising the temperature to 140°C.[48]

Postovskii and coworkers[29,51] showed for the first time that in the melt tetrazolo[1,5-*c*]benzothiazole (II) exists in equilibrium with the azido-tautomer. Wentrup[48] noted an interesting transformation of the azide at [above] its melting point into the [solid] tetrazole, which in turn is reconverted into the azide on fusion. On raising the temperature, the labile tautomeric azides, isolated under special conditions[48,133], undergo ring closure to the more stable tetrazole form (in solution or in the crystalline state).

Very low temperatures (obtaining in liquid SO_2) proved to be suitable for the preservation of the labile azido- and tetrazole tautomers[48].

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The tetrazole ring condensed with a nitrogen-containing heterocycle is in many instances readily cleaved at the $N_{(1)} - N_{(2)}$ bond with formation of the isomeric azidoazomethine derivative. Such transformations in the series of condensed tetrazoles do not require the expenditure of much energy. Therefore isomerisation frequently occurs on dissolution, heating, and sometimes after prolonged storage of condensed tetrazoles. A tautomeric equilibrium between the cyclic tetrazole and the open-chain azido-forms is frequently established as a result of such transformations and can occur in the crystalline state, in the melt, and in solution. The stability of the condensed tetrazole and the isomeric azido-form or the state of equilibrium between them is determined by the nature of the nitrogen-containing heterocycle with which the tetrazole ring is condensed and by the electronic nature of the substituent in the former, solvent polarity, pH of the medium, and temperature.

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Hetarylformazans†

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The literature data on the synthesis, structure, and properties of formazans containing heteroaromatic substituents (hetarylformazans) have been reviewed and arranged sytematically. Hetarylformazans have been compared with arylformazans in characteristic reactions such as oxidation to tetrazolium salts, alkylation, and conversion into stable verdazyl radicals. Special attention has been devoted to the coordination chemistry of formazan-containing systems and to the consideration of the characteristic features introduced by hetaryl substituents into the structure of the complexes. Various aspects of the practical applications of hetarylformazans and their derivatives (dyes, bioindicators, ligands, analytical reagents) and the prospects for the development of their chemistry have been examined.
The bibliography includes 221 references.

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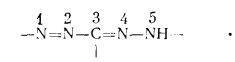
I. INTRODUCTION

Formazans[1-5] are compounds with the characteristic azohydrazone group



The compounds unsubstituted in the 1- and 5-positions and also 1,5-dialkylformazans are so far unknown. The 3-position (the *meso*-position) can contain various substituents (hydrogen, alkyl, aryl, hetaryl, halogens, CN, SH, OH, etc.).

Aromatic formazans—1,5-diphenyl and 1,3,5-triphenyl derivatives—were first described by von Pechmann and Bamberger in 1892.[1,2] However, the chemistry of formazans and the tetrazolium salts obtained from them did not begin to develop vigorously until the 1940s when Kuhn and Jerchel[6] found applications for tetrazolium salts in biochemistry and histology as indicators for oxidation-reduction processes. The successful use of formazans as dyes[3,5], ligands in complex formation reactions[7-12], and analytical reagents[5] played an important role in the development of the chemistry of formazan-containing systems.

While arylformazans have been known since the end of the past century, the first representative of hetarylformazans was described in 1951 by Ludolfy[13], who synthesised a $C_{(3)}$-substituted formazan of the pyridine series by combining a diazonium salt with uracil-4-aldehyde. However, this synthesis constituted merely an episode in a series of studies on the preparation of arylformazan derivatives and a series of systematic studies on heterylformazans was initiated by the investigations of Ried and coworkers[14-18]. These studies were stimulated by the search for blue formazans and new tetrazolium salts which might serve as indicators for the investigation of redox processes in blood[17-21]. Subsequently valuable dyes, analytical reagents, ligands, and other practically important compounds were found among hetarylformazans. All these factors led to a considerable development of the chemistry of hetarylformazan systems. During the last fifteen years (mainly in 1963–1972), more than 200 studies were published on the synthesis, physicochemical properties, structure, complex-forming capacity, and analytical applications of hetarylformazans. This review deals with these studies and includes the literature up to 1974.

† We have given the name hetarylformazans to formazans containing heteroaromatic substituents in the 1-, 5-, or 3-positions in the formazan group.

II. SYNTHESES OF HETARYLFORMAZANS

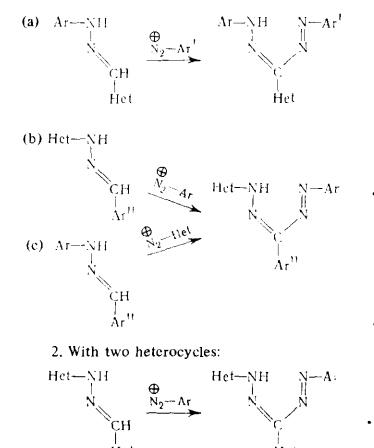
1. The Coupling of Diazo-compounds with Hydrazones (Ried's Method)[1]

The most widely used method for the synthesis of formazans is the coupling of diazonium salts with hydrazones in an alkaline medium[1-5]. Ried developed an amost exhaustive scheme of synthetic pathways for all possible hetarylformazans based on the coupling of aryl- or hetaryl-diozonium salts with various hydrazones (Scheme 1).

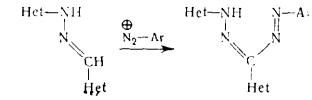
Scheme 1

Ried's syntheses of hetarylformazans

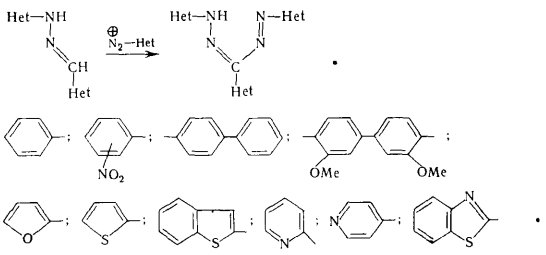
1. With one heterocycle:



2. With two heterocycles:

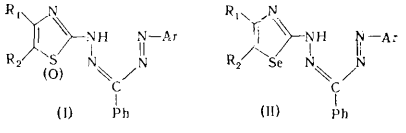


3. With three heterocycles:



The syntheses of formazans containing a heterocycle at the meso-carbon atom, i.e. based on heterocyclic aldehydes (method 1 in Ried's scheme), were developed further. Thus, in order to investigate the biological activity of formazan and tetrazolium salts, Cottrell et al.[22] obtained a group of formazans containing 4-pyridyl, 2-furyl, and 2-phenyl-2,1,3-triazolyl substituents in the *mesc*-position. Pyridine derivatives were synthesised to test them as potential antitubercular agents, since there is some structural similarity between 3-pyridylformazans and 5-pyridyltetrazolium salts on the one hand, and isonicotinic acid hydrazide (isoniazide) on the other.

The syntheses of 1-hetarylformazans developed extensively on the basis of Ried's studies (methods 1b and 2 in Scheme 1). Beyer, Pyl, and coworkers[23-26] described 1-azolylformazans containing thiazole, oxazole (I), and selenazole (II) residues. In their study of the properties of heterocyclic hydrazino-derivatives, they synthesised benzylidenehydrazones and then, via coupling the latter with aryldiazonium salts, they obtained formazans. 1-Thiazolylformazans were also obtained by specific synthesis from thiazolyldiazonium salts and aromatic hydrazones:

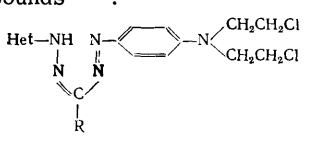


R_1 and R_2 = H, Me, Ph; R_1 = Ph, Me; R_2 = Ph, COOEt

In the study of formazans of this type, the main aim was the preparation of tetrazolium salts suitable for the investigation in enzymohistology.

In order to study the relation between the structure and properties of formazan-containing systems, 1-(1-alkylbenzimadazol-2-yl)-3-methyl-5-phenylformazans with different substituents in the benzene ring[27], 1-benzothiazolyl- and 1-benzoxazolyl-formazans[28-31], and also derivatives containing tetrazole[32-36], triazole[37], or naphthothiazole[38, 39] residues in the 1-position of the formazan group were obtained.

Heterocyclic formazans containing cytotoxic and bis-(β-chloroethylamino)-groups were obtained as potential antitumour compounds[40-41]:

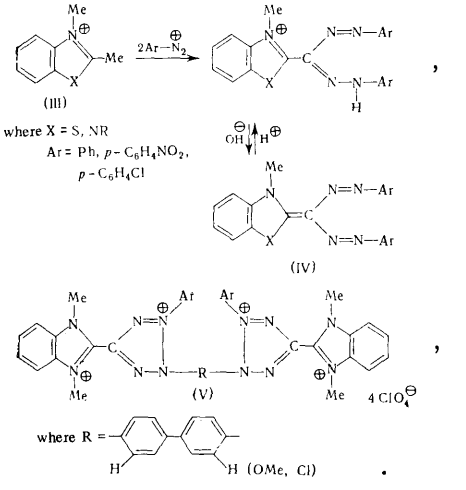


where Het = phenyltetrazolyl, 1-methylbenzimidazol-2-yl, or 1,5,6-trimethylbenzimidazol-2-yl and R = Me or Ph.

To investigate their antibacterial and complex-forming properties, formazans derived from benzimidazole with a sulphamoyl group in the phenyl substituent were synthesised[42]. 1-Benzazolyl-3-methyl-5-phenylformazans containing a sulpho-group in the phenyl residue, introduced to increase the solubility of the compound in water, can be used as analytical reagents[43]. 1-Hetaryl-3,5-diphenylformazans (hetarylthiazoloyl, benzothiazolyl, α-pyridyl, nitropyridyl, and other derivatives) were synthesised and investigated[44-46] as reagents for the determination of a number of metal ions. A series of 1-benzothiazolyl-3,5-diphenylformazans with halogeno-, methyl, and alkoxy-groups as substituents in the 6-position of the heterocyclic ring were synthesised for this purpose[47,48].

2. Azo-coupling with Compounds Containing an Active Methyl Group (the Wahl-Le Bris Method[3])

3-Hetarylformazans can be synthesised not only from aldehydes, but also from heterocycles in which the methyl group has been activated by the quaternisation of the nitrogen atom of the heterocycle[3]. Thus Wahl and Le Bris[49-52] used in the synthesis of 3-benzazolylformazans the quaternary ammonium salts of 2-methylbenzothiazole or 2-methylbenzimidazole (III), which yielded hydrazones (one mole) or "pseudoformazans" (IV) (2 moles) on coupling with diazonium salts. In an acid medium the pseudoformazans exhibited all the properties of formazans, gave rise to deeply coloured chelate complexes with metals, and on oxidation were converted into colourless tetrazolium salts. Bisformazans, obtained by the successive coupling of 1,2-dimethylbenzimidazolium methiodide, initially with phenyldiazonium salts and then with bisdiazobenzidine, had a blue colour and were readily oxidised to colourless bistetrazolium salts (V).[53,54] The authors proposed these salts as histochemical reagents.



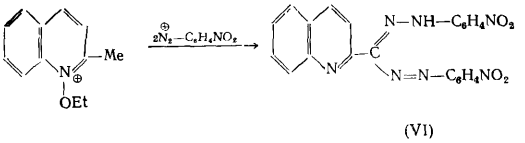
where X = S, NR; Ar = Ph, p-$C_6H_4NO_2$, p-C_6H_4Cl

(IV)

(V)

where R = H (OMe, Cl)

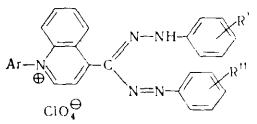
Using the mobility of the hydrogen atoms in the α-methyl groups of the heterocycles (the Porai-Koshits rule), Mishina and Efros[55] obtained a group of 3-hetarylformazans (VI). The quaternary salts of quinaldine or lepidine N-oxide were introduced into the azo-coupling reaction:



(VI)

The ability of the quaternary salts of *N*-oxides to enter into the azo-coupling reaction depends on the structure and basicity of the heterocycle. Thus the quaternary salts of α- and γ-picoline *N*-oxides proved to be incapable of reacting in this way. 9-Methylacridine and its *N*-oxide form only the hydrazone on coupling with diazonitroaniline, while 9-methylphenanthridine is readily converted into 3-phenanthridinylformazan[55].

Pilyugin and coworkers[56-62] synthesised and investigated a series of 3-hetarylformazans (VII). 1-Aryl-lepidinium or arylquinaldinium perchlorates undergo azo-coupling with various diazo-compounds, yielding formazans. On the other hand, the reaction with 1-alkyl-lepidinium salts stops at the hydrazone stage. The structure of the resulting formazans (VII) was demonstrated by the stepwise synthesis of asymmetric formazans (R′ ≠ R″):

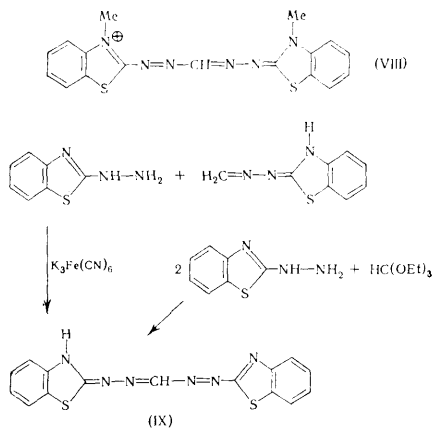


(VII) ,

where R′ and R″ are groups with different electronic effects in the *ortho*-, *meta*-, or *para*-positions.

3. Oxidative Azo-coupling (the Hünig Method[63])

Symmetrical 1,5-dihetarylformazans, which are missing from Ried's scheme, appeared at the beginning of the 1960s. Hünig quotes the synthesis of 1,5-dibenzothiazolylformazan as an example of oxidative azo-coupling. The Hünig reaction is based on the fact that, in an acid medium in the presence of $K_3Fe(CN)_6$ as an oxidant, amidrazone systems (hydrazine derivatives in the hydrazone form) can undergo the electrophilic coupling reaction with azo-components, forming azodyes, or tetraazapentamethine-cyanine dyes (VIII). Numerous studies by Hünig and coworkers, begun in 1957, have been summarised in a review[63]:



In 1963 Hünig[64] obtained the product of the oxidative coupling of 2-hydrazinobenzothiazole and its formaldehyde hydrazone (IX), which was called 1-(benzothiazol-2-yl)-5-(benzothiazolin-2-ylidene)-1,2,4,5-tetraazapenta-1,3-diene. The structure of the compound was demonstrated by a specific synthesis from 2-hydrazinobenzothiazole and orthoformic ester. However, Hünig does not describe studies on the tautomerism and properties of this compound in relation to the properties of formazans and hence its characteristics as a 1,5-dibenzothiazolylformazan.

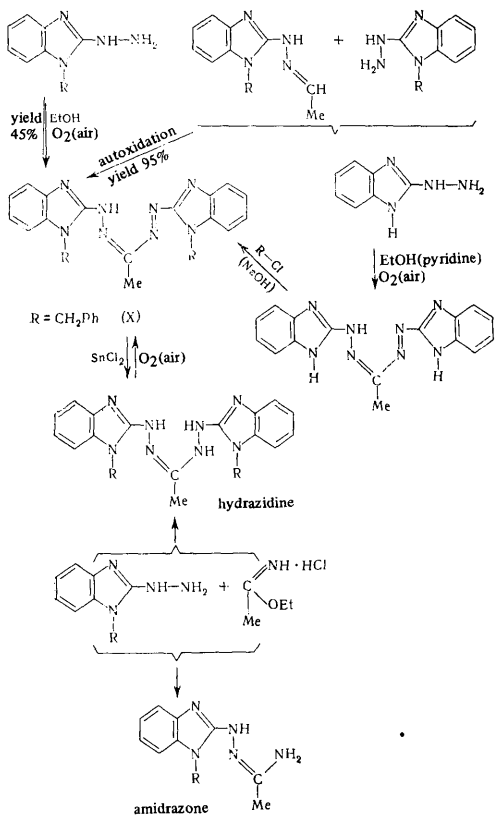
4. Autoxidation of Hetarylhydrazines (the Bednyagina–Postovskii Method[66,70])

Simultaneously with Hünig's studies, the syntheses of 1,5-dibenzimidazoylformazans were described. It was observed in 1960 [65] that alcoholic solutions of 1-alkyl-2-hydrazinobenzimadazoles become dark-violet in air and on standing give rise to large violet crystals of unknown dyes with a green lustre. In the study of the molecular structures of the dyes considerable difficulties arose owing to their ability to form stable solvates with water and alcohol. On varying the 1-alkyl-2-hydrazinobenzimidazoles employed (alkyl = methyl, ethyl, benzyl, or phenyl) and the primary alcohols taken for the autoxidation (methanol, ethanol, and 1-butanol), a series of dyes were obtained. The involvement of the alcohol in the formation of the dye molecule was established and it was shown that the dyes have the structure of the hitherto unknown 1,5-di-(1-alkylbenzymidazol-2-yl)-3-alkylformazans[66]. The autoxidation probably involves several reactions with different mechanisms. Thus oxygen is absorbed rapidly (in the first 30 min) and the colour develops slowly (in 24 h). The rate-limiting stage (the autoxidative coupling) is nucleophilic, since it is catalysed by bases (pyridine) and is inhibited by Lewis acids. Thus, despite its outward similarity to the Hünig reaction, the autoxidation reaction differs significantly from it as regards conditions and mechanism.

The first group of symmetrical 1,5-dibenzimidazolylformazans containing an alkylated or arylated benzimidazole ring was described in 1964.[66,67] 2-Hydrazinobenzimidazole unsubstituted at the nitrogen atom is more acidic and resistant to autoxidation. Formazans based on it can all be obtained by autoxidation in an alcohol–pyridine medium[68]. Formazans unsubstituted at the *meso*-carbon atom have been obtained in two ways to confirm their structure: by autoxidation in methanol and by condensation of hetarylhydrazines with orthoformic ester[66,67]. One of the alkyl-substituted formazans, namely 1,5-di-(1-benzylbenzimidazol-2-yl)-3-methylformazan (X), was obtained by several independent syntheses (Scheme 2), in addition to the autoxidation reaction, which left no doubt about its structure[69,70]. When 1-benzyl-2-hydrazinobenzimidazole was allowed to react with the hydrochloride of acetimidoethyl ether, colourless products—a hydrazidine (in the presence of a deficiency of the iminoether) and an amidrazone (for a 1 : 1 reactant ratio)—were isolated (similarly to the reaction in the series of arylhydrazines[71,72]) in addition to the formazans. It was shown that, the formazan ⇌ hydrazidine oxidation-reduction transitions take place fairly readily.

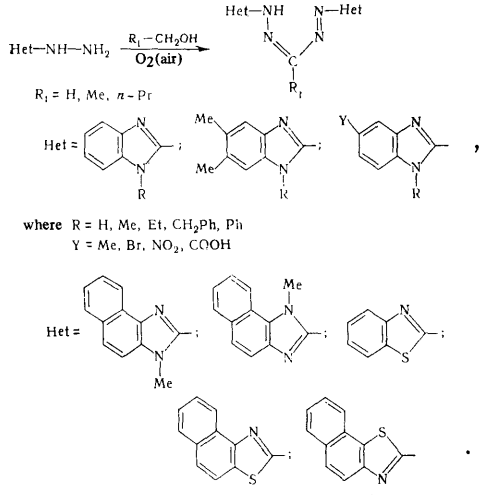
Scheme 2

Syntheses of 1,5-di(1'-benzylbenzimidazol-2'-yl)-3-methylformazan



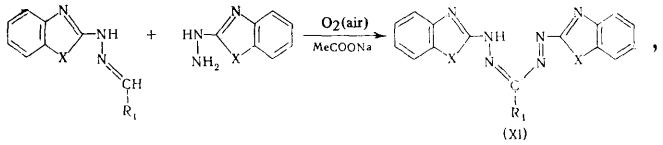
Scheme 3

Synthesis of 1,5-dibenzazolylformazans and 1,5-dinaphthazolylformazans



Other hydrazinobenzazoles or hydrazinonaphthazoles are also capable of spontaneous oxidation and conversion into the corresponding 1,5-dibenzazolylformazans or 1,5-dinaphthazolylformazans (Scheme 3). Thus 2-hydrazinonaphtho[1,2-*d*]imidazole and its 1-methyl- or 3-methyl-substituted derivatives yielded the corresponding 1,5-dinaphthimidazolylformazans in methanol, ethanol, or 1-butanol solutions[73]. 1,5-Di{naphtho[2,1-*d*]thiazolyl}-3-methylformazan was obtained from 2-hydrazinonaphtho-[2,1-*d*]thazole in ethanol[38]. The autoxidation of 2-hydrazinobenzimadazoles substituted in the 5-position proceeds smoothly. 1,5-Di-(1-benzylbenzimazol-2-yl)-3-methylformazans containing methyl, bromo-, methoxy-, nitro-, or carboxy-groups in the benzene rings were obtained in this way[74]. On autoxidation in ethanol, 2-hydrazino-1,5,6-trimethylbenzimidazole or 1-benzyl-2-hydrazino-5,6-dimethylbenzimadazole give rise to beautiful large violet crystals of 1,5-di[1,5,6-trimethylbenzimadazol-2-yl]3-methylformazan or 1,5-di-[1'-benzyl-5,6-dimethyl-benzimadazol-2-yl]-3-methylformazan[75,76].

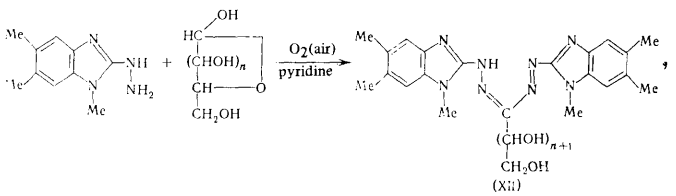
The yields of formazans do not usually exceed 40%. Deeply coloured resins are formed as side products. 1-Alkylbenzimidazoles can be always isolated in 10% yield from the colourless products of the autoxidation of 1-alkyl-2-hydrazinobenzimidazoles. In autoxidation in an alkaline medium (NaOH, pH > 10) nitrogen is evolved and the yield of 1-alkylbenzimidazole rises to 50%. Since 1-alkyl-benzimidazolones were not detected among the side products, the formation of an intermediate diazohydrate appears to be unlikely. It is suggested that 2-benzimidazolyldi-imine and a hydrazone, produced as a result of the oxidation of the alcohol to the aldehyde, are formed as intermediates[70]. The experimental observation that 1-alkyl-2-hydrazinobenzimidazole and its hydrazone with acetaldehyde, taken in equimolecular proportions, give rise to a formazan in a nearly quantitative yield constitutes convincing proof that the autoxidation reaction proceeds via a stage in which a hydrazone is produced. This reaction was extended to other heterocyclic and aromatic hydrazones. A convenient method for the synthesis of 1,5-dibenzalolylformazans (XI) was developed[77]. It consists in the joint autoxidation of 2-hydrazinobenzazoles with their aldehyde-hydrazones in solution in the alcohol corresponding to the aldehyde to which sodium acetate had been added:



where R_1 = H, Me, or n-Pr and X = NH, NMe, NEt, NCH_2Ph, NPh, or S.

In certain cases it is possible to employ a version of the method which involves the joint autoxidation of the hydrazino-derivative and the aldehyde, without the isolation of the intermediate hydrazone, in pyridine solution.

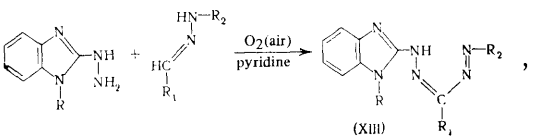
Symmetrical benzimidazolylformazans (XII) containing sugar residues in the 3-position were obtained in this way[78]. The formazans are of interest as structural fragments of vitamin B_{12}:



(XII)

where the sugar is D-ribose, L-arabinose, or glucose.

1-Alkyl-2-hydrazinobenzimidazoles, which undergo autoxidation particularly readily, can undergo autoxidative coupling in pyridine–water solutions with a wide variety of hydrazones, including aromatic hydrazones[79]. Mono-, di-, and tri-hetarylformazans (XIII), including asymmetric formazans, containing various benzazole residues in the 1- and 5-positions (benzimidazole–benzothiazole or benzimidazole–benzoxazole) were obtained in this way:



(XIII)

where R_1 = Me, Ph, or quinoxalin-2-yl and R_2 = Ph, p-$C_6H_4NO_2$, benzothiazol-2-yl, benzoxazol-2-yl, or 1-phenyltetrazol-5-yl.

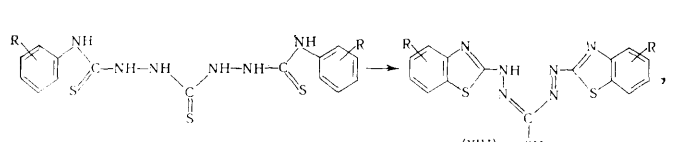
Symmetrical benzazoyl formazans containing the phenyl group in the 3-position were synthesised in the same way[80]. However, autoxidative coupling of 1-benzyl-2-hydrazinobenzimidazole with arylhydrazones of nitroformaldehyde led to the formation of 1-(1-benzylbenzimidazol-2-yl)-5-arylformazans unsubstituted at the *meso*-carbon atom instead of the expected 3-nitroformazans[81].

Thus the syntheses of 1-hetaryl- or 1,5-dihetarylformazans can be based on 2-hydrazinobenzimidazoles, 2-hydrazinobenzothiazoles, or the corresponding naphtho-derivatives, which are all capable of autoxidation. The range of hydrazines capable of autoxidation can probably be extended.

5. Other Methods

Formazans containing non-aromatic heterocycles in the 3-position can be obtained by the introduction of the heterocycle into the finished formazan. Thus, 3-piperidinyl- and 3-morpholinyl-formazans were synthesised from 3-chloro-1,5-diphenylformazan[82] and pyrrolidino-, piperidino-, and morpholino-methyl derivatives were obtained from arylformazans[83] or 1,5-dibenzimidazolylformazans[67] unsubstituted in the *meso*-position.

Pel'kis and coworkers[84,85] obtained 1,5-dibenzothiazol-yl-3-mercaptoformazans (XIV) by the closure of the benzothiazole ring in the almost completed formazan molecule:



(XIV)

where R = H, Me, OEt, or Cl.

The oxidative cyclisation of 1,5-di(phenylthiocarbamoyl) thiocarbonyldihydrazides was carried out in alcoholic alkaline solutions by treatment with potassium hexacyanoferrate(III). The compounds obtained are deeply coloured crystalline substances (λ_{max} = 530–550 nm). They can exist in several tautomeric forms, but on methylation with methyl iodide they give rise to *S*-methyl derivatives. 1,5-Dibenzothiazolyl-3-mercaptoformazan is of interest as the first heterocyclic analogue of dithizone described in the literature.

It follows from the data quoted above that reliable methods have now been developed for the preparation of $N_{(1,5)}$ and $C_{(3)}$-substituted hetarylformazans. Methods involving the coupling of diazo-compounds with hydrazones and the autoxidation of hetarylhydrazines are the most general for the synthesis of hetarylformazans. While the former method is convenient for the preparation of 1(5)-hetaryl- and 1,3-dihetaryl-formazans, the latter can be used to synthesise symmetrical 1,5-dihetarylformazans. At the same time a modification of the second method, making use of the capacity of the readily oxidised hydrazinobenzazoles to undergo oxidative coupling with hydrazones[79], makes it possible to obtain asymmetric formazans, and, what is particularly important, derivatives with various heterocycles in the 1- and 5-positions of the formazan group.

The Wahl–Le Bris and Hünig methods are of limited applicability: the former can be used to prepare $C_{(3)}$-hetaryl-substituted derivatives and the latter is mainly employed for the synthesis of *NN*-dihetaryl-substituted formazans.

Five-membered monoheteraromatic systems (thiophen, furan), six-membered heterocycles (pyridine, quinoline, azines[86,87]), azoles, and their benzo-analogues have been introduced into the formazan group as hetaryl substituents.

III. THE STRUCTURE OF FORMAZANS

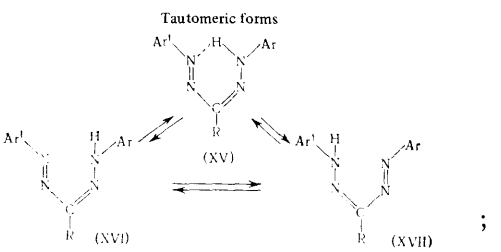
1. Arylformazans

A number of studies have been made on the tautomerism, stereoisomerism, and the state of the hydrogen bond in arylformazans[88–95]. Special studies have been carried out on the infrared spectroscopy of arylformazans[96–106], including a systematic comparative investigation of the infrared spectra of triarylformazans in relation to hydrazones, tetrazolium salts, complexes, and verdazyl radicals[102–104]. The relations between the structure and colour of formazans have been studied[107,108]. Quantum-mechanical calculations on the π-electron systems and the electronic spectra of formazans have been published[109–114].

The isomerism of arylformazans presupposes the existence of three tautomeric (XV–XVII) and four stereoisomeric (XVIII–XXI) forms (*cis-trans* with respect to the N–N bond and *syn-anti* with respect to the C–N bond) (Scheme 4).

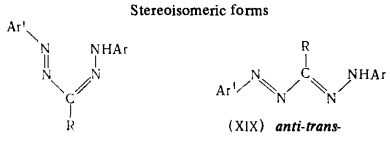
Scheme 4

Tautomeric forms



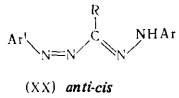
(XV) (XVI) (XVII)

Stereoisomeric forms

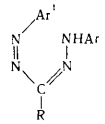


(XVIII) *syn-trans*

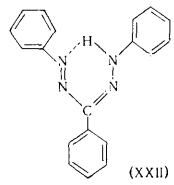
(XIX) *anti-trans-*



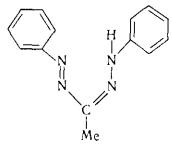
(XX) *anti-cis*
(R = Ph; Me; H)



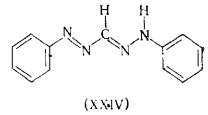
(XXI) *syn-cis*



(XXII)



(XXIII)



(XXIV).

The structure of the formazan chain is influenced significantly by the substituent R in the *meso*-position. The phenyl group usually promotes the fixation of the chelate form. The alkyl substituent (other than t-butyl[115]) weakens the hydrogen bond and leads to the opening of the chelate ring, while hydrogen stabilises the *anti-trans*-structure.

Triphenylformazan has a quasiaromatic chelate ring (XXII) with a strong intramolecular hydrogen bond[88,93,94,116], which is confirmed by the absence of the ν(NH) band in the region 2500–3200 cm^{-1} from the infrared spectra of both crystals and solutions.

The ring is so stable that it is not opened even in alkaline medium although the introduction of a nitro-group in the 1- or 5-position in the phenyl group leads to a weakening of the intramolecular hydrogen bond, which is manifested in a capacity to be converted into the sodium salt[108]. The (XVI) $\rightleftharpoons$ (XVII) tautomerism of such asymmetric formazans has been demonstrated by an isotopic method[117].

3-Methyl-1,5-diphenylformazan has an "open" structure, is more coloured than triphenylformazan [λ_{max} = 430 nm for (XXIII) and 494 nm for (XXII)], its infrared spectrum contains the ν(NH) band (3360 cm^{-1} in chloroform), and it readily forms a sodium salt in solution[2]. According to Zeif et al.[111], it has the *cis-trans*-configuration in solution without an intramolecular hydrogen bond [structure (XXIII)].

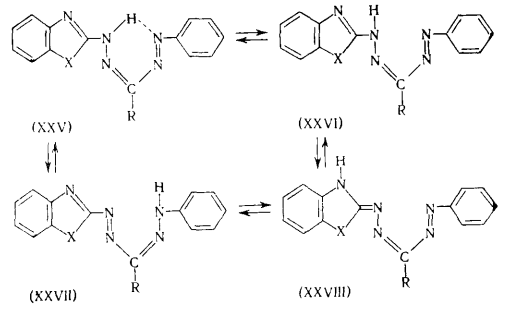
The configuration of the molecule and the nature of the hydrogen bond in diphenylformazan were recently determined by X-ray diffraction[118]. It was found that in the crystalline phase diphenylformazan has an open *anti-trans*-structure with intermolecular hydrogen bonds; according to other data[110,111], diphenylformazan retains the *anti-trans*-structure (XXIV) also in solutions.

Triphenylformazan has the chelate *syn-trans*-structure (XXII) both in solutions and apparently in the crystalline state. This is indicated by the experimental hydrogen bond energies[119] (7 kcal $mole^{-1}$ for triphenylformazan and 2.7 kcal $mole^{-1}$ for diphenylformazan) determined experimentally from the heats of combustion and also from the electronic spectra[111] and the calculation of the energy of the stabilisation of the ring by the hydrogen bond in solution (8.7 kcal $mole^{-1}$).

2. Hetarylformazans

The structure of 1-benzazolylformazans has been studied systematically in the series of hetarylformazans[27-31,108-112,120-122]. The number of possible tautomeric and isomeric forms in the series of hetarylformazans is greater than in the aromatic series. Thus the tautomeric forms (XXV)–(XXVIII) (Scheme 5) are possible for the asymmetric 1-benzazolyl-5-phenylformazans. On the other hand, the number of theoretically possible stereoisomers increases to 16 (on the assumption that the molecule is coplanar). Among these, account has been taken[110,111] of the most probable *syn-trans*- (with or without allowance for the intramolecular hydrogen bond) and linear *anti-trans*-structures.

Scheme 5



(XXV) (XXVI) (XXVII) (XXVIII).

The state of tautomeric equilibrium involving benzazolylformazans depends both on the *meso*-substituent and on the nature of the heterocycle (acidity, basicity, aromaticity) (Table 1).

Table 1. Spectroscopic characteristics and acid pK_a values of 1-benzazolyl-3-R-5-methylformazans.

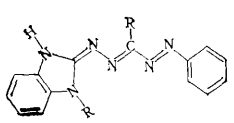
Compound	X	R	ν(NH), cm^{-1} (in CCl_4)	λ_{max}, nm (in n-heptane)	pK_a
(XXIX)	N—$CH_2C_6H_5$	Me	3450	452	12.5
(XXX)	N—$CH_2C_6H_5$	Ph	3445	454	12.1
(XXXI)	S	Ph	absent	492	11.1
(XXXII)	O	Ph	absent	475	11.2
(XXXIII)	S	Me	3450; 3360	445	9.1
(XXXIV)	O	Me	3450; 3370	415	9.7

The ν(NH) bands in the infrared spectra have been assigned on the basis of experimental[109,120] and calculated[110] (Hückel's molecular orbital method) data [correlation between π-electronic charge on the nitrogen atom linked to the proton and the ν(NH) wavenumber]: the high-frequency band (~3450 cm^{-1}) was assigned to the imino-form (XXVIII) and the low-frequency band [~3360 cm^{-1}, coinciding with ν(NH) for 3-methyl-1,5-diphenylformazan] was assigned to the amino-form (XXVI). The ν(C=N) infrared bands, with wavenumbers in the range 1510–1630 cm^{-1} for the chelate forms of formazans and 1555–1580 cm^{-1} for the open-chain forms[103,110,112], are also striking [following Kukushkina et al.[105] these bands were assigned to ν_{as}(–N=C–N)].

The long-wavelength band in the visible spectrum in the range 400–500 cm ($\pi \rightarrow \pi^*$ transition) constitutes a convenient criterion for the comparison of the structures of formazans. In the series of benzazolylformazans the chelate forms (XXXI) and (XXXII) have a deeper colour to the extent of 50–60 nm (Table 1) than the corresponding open-chain forms (XXXIII) and (XXXIV). It has been established[110,111] that in the spectra of formazans with the *anti-trans*-configuration this band exhibits a higher extinction, although it is displaced towards shorter wavelengths compared with the chelate forms.

Calculations (by the Pariser–Parr–Pople method) on the π-electron system of formazans (XXIX)–(XXXIV),[111,112] comparison of the experimental and calculated spectra (the energies and oscillator strengths of various electronic transitions), and the determination of the relations between the reactivity indices, the spectra, and the properties of formazans led to the following conclusions.

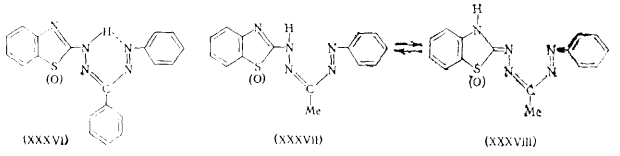
(a) Regardless of the *meso*-substituent, 1-benzimidazolyl-3-methyl(phenyl)-5-phenylformazans (XXIX) and (XXX) have (in heptane, dioxan, and carbon tetrachloride) the open-chain imino-structure and the *anti-trans* chain configuration (XXXV).



(XXXV)

The exceptional behaviour of 1-benzimidazolylformazans (the lack of an effect of the *meso*-substituent on the tautomeric shift) has been explained by the greater basicity of benzimidazole and a tendency towards the transition to imino-systems with an exocyclic double bond.

(b) Benzothiazolyl- and benzoxazolyl-formazans (XXXI)–(XXXIV) exhibit the behaviour discovered in the series of arylformazans, i.e. compounds (XXXI) and (XXXII) with a phenyl substituent in the *meso*-position have a chelate structure, like triphenylformazan. In heptane they assume the *syn-trans*-amino-configuration (XXXVI) with a weak intramolecular hydrogen bond, which dissociates even as a result of the solvating action of solvents [ν(NH) = 3200 cm^{-1} in dioxan]. A *syn-trans*-configuration with a rapid proton transfer and equilibrium between the amino- and imino-forms (XXXVII) $\rightleftharpoons$ (XXXVIII), is characteristic of the formazans (XXXIII) and (XXXIV) with the methyl group in the *meso*-position in heptane or carbon tetrachloride solutions:



(XXXVI) (XXXVII) (XXXVIII)

The changes in acidity[120] are consistent with the above conclusions. As was to be expected, the benzimidazolylformazans (XXIX) and (XXX) have pK_a values of the same order of magnitude (Table 1). In the series of benzothiazolyl- and benzaxolyl-formazans (XXXI)–(XXXIV) the proton mobility depends on the *meso*-substituent. Hydrogen bound in the intramolecular hydrogen bond is less mobile and the chelate formazans (XXXI) and (XXXII) differ from the non-chelate forms (XXXIII) and (XXXIV) by having an acid strength weaker by one–two orders of magnitude (Table 1). The *meso*-substituent has similar effects on the structure of the formazan chain in 5-aryl-1-(1-phenyltetrazolyl)formazans[32,35] and 1-naphthothiazolyl-5-phenylformazans[38,39]

The influence of the nature of the heterocycle on the colour of 1-hetarylformazans is different in the series of "open-chain" and chelate structures[70]. The colour of the "open-chain" 1-benzazolyl-3-methyl-5-phenylformazans (in benzene or heptane) depends on the basicity of the heterocycle, while in chelate formazans the determining factor is the aromaticity of the heterocycle. Formazans with the chelate structure have in general a deeper colour than those with an "open-chain" structure (Tables 1 and 2).

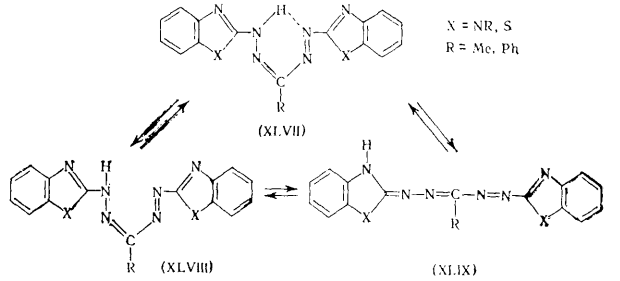
Table 2. Characteristics of 1-benzazolyl-3-R-tolylformazans.

Compound	R	X	Tolyl	M.p., °C	ν(NH), cm^{-1} (in CCl_4)	λ_{max}, nm (in alcohol)
(XXXIX)	Me	NCH_2Ph	*para*	121—124	3445	460
(XL)	Me	NCH_2Ph	*ortho*	85—87	3445	456
(XLI)	Me	S	*para*	136—137	3435; 3340	414
(XLII)	Me	S	*ortho*	81—87	3435; 3340	414
(XLIII)	Me	O	*para*	115—116	3440; 3355	400
(XLIV)	Me	O	*ortho*	80—82	3440; 3355	400
(XLV)	Ph	S	*ortho*	195—198	3425	470
(XLVI)	Ph	O	*ortho*	182—184	3421; 3321	432

The *ortho*-substituent in the benzene ring (methyl[30], halogen[31]) does not affect the structure of the formazan chain in the series of "open-chain" 3-methyl-substituted derivatives. Thus the *ortho*- and *para*-isomers of 1-benzazolyl-3-methyl-5-tolylformazans are spectroscopically indistinguishable (Table 2). However, steric hindrance by the *ortho*-substituent affects the complex-formation reactions[30] or the conversion into tetrazolium salts[31]. In contrast to this, in the series of chelate 3-phenylformazans the steric hindrance of the *ortho*-substituent is clearly manifested in the opening of the chelate ring of (XLV) and (XLVI).[123] The naphthyl residue has an effect similar to that of the *ortho*-tolyl substituent[123].

The introduction of an electron-donating (NMe_2) or an electron-accepting (NO_2) substituent into the *para*-position of the benzene ring has a particularly marked influence on the structure and colour of formazans[124]; a bathochromic effect is observed in both cases.

In the series of symmetrical 1,5-dibenzazolylformazans three tautomeric forms are possible: the chelate form (XLVII) and the "open-chain" amino-form (XLVIII) and imino-form (XLIX):

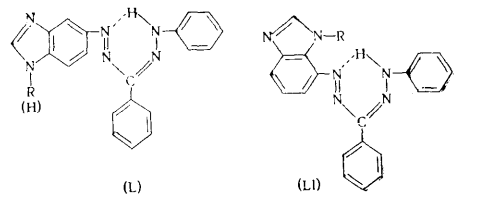


(XLVII) (XLVIII) (XLIX)

Regardless of the substituent in the 3-position (methyl, phenyl), the tautomeric imino-form of 1,5-dibenzimidazolylformazan (XLIX) has been detected in solutions [ν(NH) = 3420 and 3468 cm^{-1} in chloroform].[80] The infrared spectra of benzothiazolylformazans do not contain the ν(NH) band and they probably have the chelate structure (XLVII). Thus in the series of both symmetric and asymmetric

formazans benzothiazolyl derivatives exhibit a greater tendency towards the formation of chelate forms, while benzimidazolyl derivatives tend to form the open-chain imino-forms. The alkyl groups in the benzimidazole ring as well as those at the *meso*-carbon atom of 1,5-dibenzimidazolylformazans do not have a significant influence on the structure and colour of the formazan[66,125]. The mobility of the proton in these formazans is greater than in the asymmetric compounds (pK_a = 9.5–10.5). They are amphoteric and also exhibit a considerable basicity (pK_a = 4–5). The contribution of the imino-form with a cyanine chain is also responsible for the greater dipole moment of 1,5-di-(1-benzylbenzimidazol-2-yl)-3-methylformazan (4.9 D) compared with 1-(benzylbenzimidazol-2-yl)-3-methyl-5-(*p*-tolyl)formazan (2.7 D) or the chelate triphenylformazan (1.73 D).[70,126]

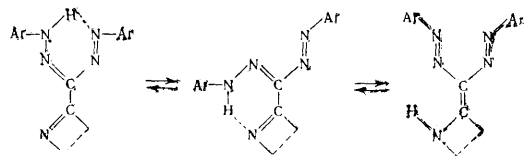
The structure of hetarylformazans in which the benzazole ring is not involved in tautomeric transformations is analogous to that of arylformazan derivatives. 1-(Benzimidazol-5-yl)-3,5-diphenylformazan (L) and 1-(1-benzylbenzimidazol-7-yl)-3,5-diphenylformazan (LI) have a chelate structure like 1,3,5-triphenylformazan (XXII).[127,128]



(L) (LI)

The replacement of the phenyl group in the *meso*-position by the methyl group leads to the opening of the chelate ring. When the benzimidazole ring is unsubstituted, the hydrogen atom attached to the pyrrole nitrogen atom can participate in intermolecular hydrogen bonds (L, R = H) and can form an intramolecular hydrogen bond with a nitrogen atom of the formazan group (LI, R = H).[128]

The tautomerism and isomerism in the series of 3-hetarylformazans has not been studied. Nevertheless in this case too there is a possibility of the existence of a series of tautomeric forms, for example:



The –N=C– fragment can form part of the pyridyl, benzazolyl, or another heterocyclic substituent with a "pyridine" nitrogen atom.

3-Benzothiazolyl-1,5-diphenylformazan does not form a sodium salt and the spectra of its solutions do not contain the ν(NH) band[29,122,129]. The data quoted, although limited, confirm that 3-hetarylformazans do not belong to systems with rapid proton transfer and in all probability give rise to chelate forms.

Thus the structure and tautomerism of hetarylformazans are mainly determined by the mode of fixation and position of the heterocyclic substituent in the formazan ring. 2-Benzazolylformazans are involved in complex tautomeric transformations, in which the state of equilibrium depends not only on the nature of the *meso*-substituent, but also on the nature and properties (basicity, acidity, and aromaticity) of the heterocycle. Similar features should probably be observed also for hetarylformazans, containing azoles and six-membered heteroaromatic systems (pyridines, azines, etc.) as the heterocyclic substituents, while the structure of hetarylformazans derived from five-membered systems with one heteroatom (furan, thiophen, pyrrole, and their benzo-analogues) should be close to those of arylformazans. However, there are virtually no experimental data concerning the tautomerism of these types of hetarylformazans.

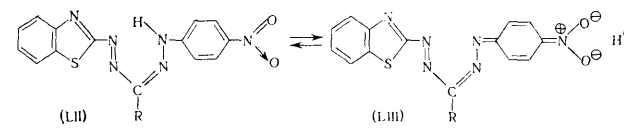
3. Photochromism and Thermochromism

Aryl- and hetaryl-formazans can in many cases isomerise by photoinduction or thermoinduction with proton transfer, which entails a change in the chromophoric system and the colour of the compound. The photochromism of arylformazans has been described by Kuhn and coworkers[89–94]. When a benzene solution of triphenylformazan is illuminated with visible light, the red chelate *syn-trans*-form (XV) (λ_{max} = 495 nm) undergoes reversible isomerisation to the yellow *anti-trans*-form (XIX) (406 nm). The transformation proceeds via the unstable *syn-cis*-form (XXI) and *anti-cis*-form (XX). Negative red-yellow photochromism of this type has also been observed for benzene solutions of compounds (L), which are analogues of triphenylformazan[127].

The photochromism of 1-benzimidazolyl-5-phenylformazans (XXIX) and (XXX), which occurs in chloroform or carbon tetrachloride solutions, is of a different type[120,130]. Here positive red–blue photochromism with a large (up to 200 nm) bathochromic photoinduction effect is observed. The reverse dark transition is difficult, but the initial form can be quantitatively isolated when a more polar solvent is added to the chloroform solution of the blue form. The ease of the reconversion into the initial formazan, the change in the nature of the infrared spectrum of the irradiated form, and steric hindrance by the *ortho*-substituent in the 5-phenyl group suggested[120] that photoinduction is accompanied by intermolecular proton transfer and the formation of dimeric structures.

The photochromism of mercury and zinc dithiozonates, which has been described[131,132], can also be accounted for by a change in the chromophoric system of the ligand (isomerisation and proton transfer). The isomerisation of the formazan chain similarly explains the photochromism of 5-alkyldithizones[133,134].

Substances exhibiting both negative[135,136] and positive[135,137] thermochromism have been found among the benzazolylformazans. The group of 1-benzothiazolyl-5-nitrophenylformazans (LII) has been studied in greater detail:



(LII) (LIII)

λ_{max} = 470–500 nm λ_{max} = 600–610 nm

It has been established that the repeated reversible thermochromic transitions of alcoholic solutions from the initial red form (LII) to the thermally induced blue form are due to dissociation and conversion into the anionic form (LIII), whose spectrum is identical with that of the sodium salt of the formazan. The formazan with R = Me has pK_a = 8.20 and therefore in aqueous and alcoholic solutions (pK_a = 8.15) dissociation proceeds readily as a result of thermoinduction. The formazans with R = Ph

and $CHMe_2$ are less acidic (pK_a = 8.94 and 9.53) and therefore they exhibit thermochromism in buffer solutions at pH values close to the pK_a of the formazans.

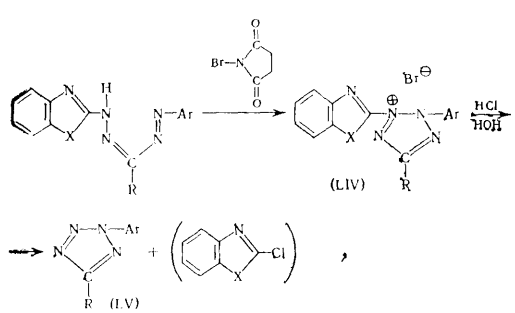
IV. PROPERTIES OF HETARYLFORMAZANS

The characteristic reactions of formazans (reversible oxidation-reduction transitions to tetrazolium salts, alkylation and conversion into verdazyl radicals, and salt and complex formation with metal ions) proceed in a specific manner in the series of hetarylformazans. 1(5)-Hetaryl- and 1,5-dihetaryl-formazans are much more labile and reactive than aryl- or 3-hetarylformazans. 1,5-Dihetarylformazans exhibit a tendency towards transitions to cyanine systems.

1. Oxidation to Tetrazolium Salts

The only method for the preparation of tetrazolium salts is oxidation of formazans. In the series of hetarylformazans the oxidation and formation of tetrazolium salts of 3-hetarylformazans has been most thoroughly investigated[1,6]. Since the stabilities of these formazans and their tetrazolium salts are comparable to those of aromatic compounds, it is possible to employ here the same oxidants, namely mercury(II) oxide, isopentyl nitrite, and lead tetraacetate. A convenient method for the oxidation by nitric acid has been proposed for 3-arylquinaldinium- and 3-aryllepidinium-formazans (VII).[58]

The oxidation-reduction properties of 1-hetarylformazans and their tetrazolium salts have so far been inadequately investigated. Owing to the instability of these formazans in an acid medium, their conversion into tetrazolium salts is carried out by Kuhn's method[138] under the influence of bromosuccinimide. Tetrazolium salts derived from thiazolyl-, oxazolyl-, and selenazolyl-formazans[24,25] and also from 1-benzozolylformazans[29,31,139] were obtained in this way. They differ from aryltetrazolium salts (LIV) by their instability, which becomes more pronounced with increase of the electronegativity of the heterocycle (on going from benzothiazole to benzoxazole). Benzoxazolyltetrazolium bromides have not been isolated at all: they are immediately cleaved with formation of 2,5-disubstituted tetrazoles[29,123] (LV). The more stable benzothiazolyltetrazolium bromides[123] and benzimidazolyltetrazolium bromides[140] are readily cleaved in acid hydrolysis, yielding the same disubstituted tetrazoles and 2-chlorobenzazoles (isolated in the case of benzimidazole[140]):

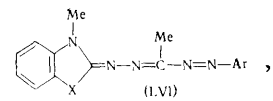


where R = Me of Ph, Ar = Ph or $\alpha(\beta)$-naphthyl, and X = NMe, S, or O.

Symmetrical, 1,5-dibenzimidazolylformazans are readily brominated by bromosuccinimide[139], but instead of tetrazolium salts they probably form bromoamines, which are themselves capable of brominating toluene or acetone.

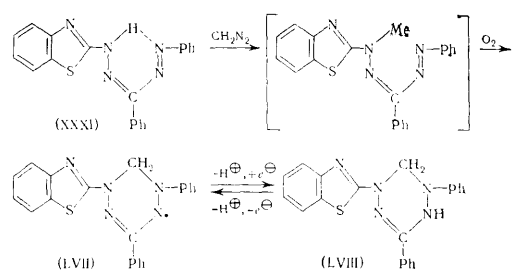
2. Alkylation and Preparation of Verdazyl Radicals

Methylation of 5-aryl-1-benzazolyl-3-methylformazans by methyl iodide in an alcoholic alkaline medium with the aim of investigating the tautomeric shifts and reactivities of asymmetric hetarylformazans led[141,142] to the formation of methyl derivatives (LVI) containing the methyl group in the benzazole ring, i.e. to the fixation of the tautomeric imino-form:



where X = NR, S, or O.

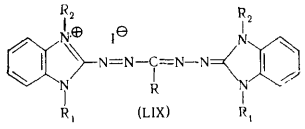
In the light of the studies of Kuhn and coworkers[143,144] and Neugebauer and coworkers[145,146] on the oxidative methylation of triarylformazans and the formation of deeply coloured stable free radicals (verdazyl radicals), the methylation of chelate hetarylformazans is of special interest. However, it was found that in the series of hetarylformazans capable of the amine–imine tautomerism, the possibility of the formation of verdazyl radicals is limited. Thus methylation of compounds (XXXI) and (XXXII) by methyl iodide yielded[142] the methyl derivatives (LVI). Only in the case of compound (XXXI), i.e. the formazan with the most aromatic heterocycle (benzothiazole) was it possible to obtain a crystalline dark-green paramagnetic substance by methylation with a benzene solution of diazomethane and autoxidation in air. Analysis, spectra (ESR and ultraviolet), and properties [capacity for the leuco-base (LVIII) ⇌ verdazyl (LVII) oxidation-reduction transitions] confirmed the structure of the compound as 1-benzothiazolyl-3,5-diphenylverdazyl (LVII):



Presumably, wider possibilities for the synthesis of verdazyl radicals will become apparent also in the series of 3-hetarylformazans or hetarylformazans in which the heterocycle is not involved in tautomerism [compounds (L) and (LI)].

Alkylation of symmetrical 1,5-dibenzimidazolylformazans proceeds in an altogether different manner. When the formazan is acted upon by an alkyl iodide in dimethylformamide, well-crystallised deeply coloured (violet) substances are formed, analysis of which shows them to be the iodides of the alkyl derivatives, while their spectra in

the visible region hardly differ from those of the hydrochlorides of the same formazans. It has been established[141] that these products are tetraazapentamethinecyanines derived from benzimidazole (LIX) and resemble Hünig's azacyanines (VIII):[69]



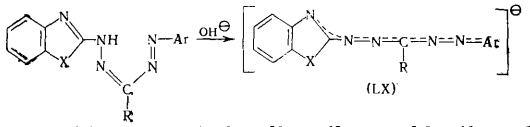
(LIX)

where R = H or Me and R_1 and R_2 = Me, Et, or CH_2Ph.

3. Acid-Base Properties and Capacity for Complex Formation

Benzazolylformazans are much more amphoteric than arylformazans. Their basicity increases owing to the presence of the benzazole ring (the "pyridine" nitrogen atom) and the acidity increases owing to tautomerism.

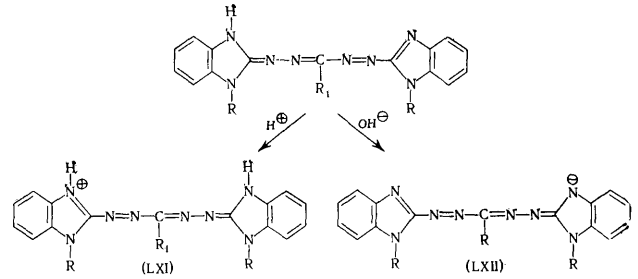
Like arylformazans, asymmetric 1-benzazolylformazans are unstable in acid media, where, after a deepening of the colour (conversion into the cation), the solution undergoes a reversible decolorisation after several minutes (cleavage, oxidation)[70]. Formazans are stable in alkaline media. The conversion into the aryl (LX) is accompanied by a bathochromic shift due to salt formation, which depends on the structure of the formazan. For each formazan, the pH at which the proton is abstracted can be readily determined spectrophotometrically (the most convenient method for the determination of approximate values of pK_a).



(LX)

The colour of the anion is hardly influenced by the substituent R in the *meso*-position. But, since the initial formazans (derived from benzothiazole and benzoxazole) have different colours depending on the *meso*-substituent, the bathochromic effect of the abstraction of a proton from the more deeply coloured chelate formazans (R = Ph) is smaller (50–60 nm), while for the "open-chain" (R = Me) compounds it is greater (100–110 nm). The colour of the anion is determined by the nature of the heterocycle (X = NR, 530–540 nm; X = S, 516–520 nm; X = O, 490–500 nm). The substituents in the benzene rings of the phenyl groups have different effects on the colour of the anion: the sulpho-group (in both *meta*- and *para*-positions) hardly alters the colour[43], while the nitro-group causes a sharp bathochromic shift[124]; the ortho-effect of substituents (methyl, halogen) is not shown[30,31].

The symmetrical 1,5-dibenzimidazolylformazans are stable over a wide pH range. They form well-crystallised salts with both hydrogen halides (monohydrohalides) and with sodium hydroxide (monosodium salts)[147]. The similarity of the absorption spectra in the visible region of the hydrochlorides and sodium salts is striking. When formazans (λ_{max} = 530–540 nm) are converted into salts, a bathochromic shift of the absorption band maximum, an increase in its intensity, and its splitting are observed (570–580 and 600–610 nm for the cation and 560–570 and 600–614 nm for the anion). It has been established[125,147] that these formazans behave in salt formation like cyanine bases and on addition or abstraction of a proton are converted into systems analogous to the onium (cation) or acihalochromic (anion) cyanine dyes. The similarity of the structures of the cation (LXI) and the anion (LXII) is responsible for their identical colour.

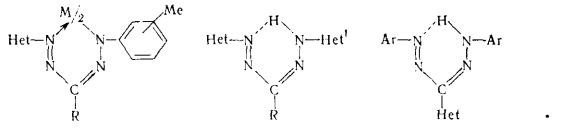


(LXI) (LXII)

The formation of complexes by 1-hetaryl- and 1,5-dihetaryl-formazans with metal ions of the 3-α-series in aqueous organic solutions proceeds just as readily as salt formation. The large bathochromic effect (100–200 nm), high sensitivity, and virtually instantaneous complex formation make these formazans (particularly benzazolylformazans) promising reagents for spectrophotometry. By varying the heterocyclic residues in the formazan molecule or by introducing additional complex-forming groups, it is possible to influence the selectivity of the ligand, the bathochromic shift, and the stability of the complex.

V. COORDINATION COMPOUNDS OF HETARYLFORMAZANS

The capacity for the formation of complexes with metals is virtually the most characteristic property of formazans. The interaction of hetarylformazans with metals leads to the formation of molecular complexes or chelate complexes with an MN_4 coordination unit. The latter has been attracting continued attention not only owing to the specific action of the ligand environment on the stereochemistry of the polyhedra of the complexes but also owing to its exceptional role in biologically important objects[70,148–153].



(LXIII) (LXIV) (LXV)

The molecular complexes $MCl_n.mL$ (n = 2 or 4, m = 1 or 2, L = formazan; M/2 can be also a hydrogen atom) were synthesised by the interaction in the cold between metal chlorides and 1(5)-hetarylformazans in acetone (MX_2) or carbon tetrachloride (MCl_4).[156] At the same time molecular complexes of $C_{(3)}$-hetarylformazans (LXV) with cobalt(II) chloride have been isolated[129] from hot ethanol. This solvent, together with acetone and dimethylformamide, has been widely used to prepare metal chelates[152–155,157–173].

The choice of salts for the synthesis of chelate complexes depends on the complex-forming metal: for copper(II), cobalt(II), and zinc(II), the best result was achieved when chlorides were employed, and for nickel, nitrates were most successful. On the other hand, bearing in mind the continued applications[148,152,153] in the synthesis of different classes of chelate complexes the method based on the interaction of metal acetates in ethanol or methanol, it should be recommended for wide-scale employment also in the synthesis of metal chelates

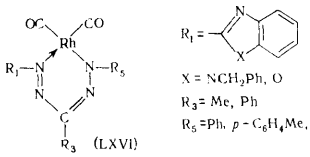
derived from formazans. We see the advantages of this method, which has already been used in a few instances[155,174] in a series of formazan-containing systems and yielded satisfactory results, also in the possibility of avoiding the formation of molecular adducts of the type $M(L-H)_2.nMX_2$, which accompanies the formation of copper chelates[162]. The formation of adducts greatly complicates the isolation of pure $Cu(L-H)_2$ complexes and requires repeated crystallisation of $Cu(L-H)_2.nCuCl_2$ from aqueous pyridine[162]. In this case pyridine apparently play the role not so much of a solvent as of an effective complex-forming agent:

$$Cu(L-H)_2 \cdot n\,CuCl_2 + n\,C_5H_5N \rightarrow Cu(L-H)_2^{+}\,n(C_5H_5N \rightarrow CuCl_2)\ .$$

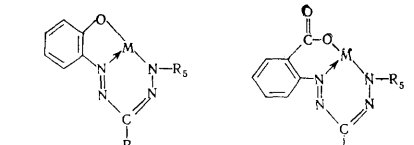
The type of complex (molecular or chelate) depends on the nature of MX_n and the conditions of synthesis.

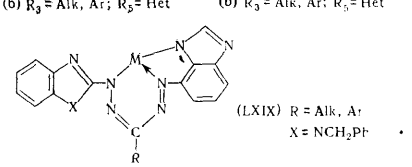
The tetrachlorides of Group IV metals form the molecular complexes $MX_4.L_n$ (n = 1 or 2).[156] Cobalt[129] and zinc[155] dichlorides give rise to complexes of a similar type under mild conditions. Bivalent transition metal and uranyl nitrates and acetates tend to form preferentially metal chelates of the type $M(L-H)_2$ or $M(L-H_2)$. At the same time, depending on the conditions of the synthesis, it is possible in a few instances to obtain complexes of both types indicated above for the same MX_n. Thus zinc chloride forms not only molecular complexes but also chelate complexes (in aqueous acetone or aqueous alcoholic media at pH in excess of 7).[70,155]

Complexes with mixed ligands may occupy a special place among formazan complexes. So far there has been only one report on this subject: dicarbonylhetarylformazanrhodium complexes (LXVI) were synthesised and their infrared absorption spectra were obtained[175].

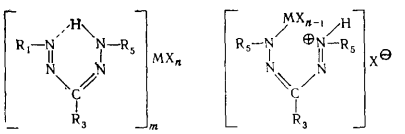


In most cases the molecular complexes have the composition $MX_n.L$ [129,153,155,156] (with the exception of the complexes of tin tetrachloride—$SnCl_4.2L$),[156] while the metal chelates have the composition $M(L-H)_2$.[152–156,162,163,166–168,174,176–178] However, an extremely characteristic feature of hydroxy- and *o*-carboxy-hetarylformazans, like that of 1-(benzimidazol-2-yl)-5-(benzimidazol-4-yl)formazan derivatives, is the formation, together with 2:1 chelate complexes[129,157–160,164,176], of 1:1 metal chelates $(ML-H)_2$ [129,157,164,165,169,172,173] [compounds (LXVII)–(LXIX) respectively].

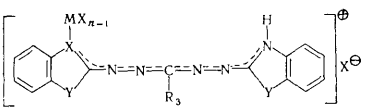




The structure of the molecular complexes was studied mainly by spectroscopic methods[70,153,155,156], while that of metal chelates was investigated in addition by the dipole moment and magnetochemical methods[153,163,166,168,174,177,178]. The compositions $MX_n.L$ and $MX_n.2L$ do not by themselves indicate the nature of the complexes formed, since ionogenic compounds such as the salts (LXXI) or the cyanines (LXXII) can have the same elemental composition as the products (LXX) of the addition of MX_n to formazans[156].



m = 1, 2; n = 2, 4;
M = Ti, Sn, Zn



Y = O, S, NR; M = Ti, Sn, Zn; X = Cl

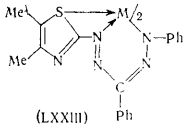
The choice between the above structures in favour of (LXX) [156] for MCl_4 and (LXXII) [155] for $ZnCl_2$ was based on ultraviolet and infrared spectroscopic data and dipole moments. The infrared spectra of $MCl_4.L$ and $MCl_4.2L$ do not contain the absorption bands of the immonium group (NH^+), which would have been expected for the ionic structure of (LXXI). The dipole moments of the compounds (8–10 D) also support molecular complexes of type (LXX).[156] On the other hand, the $ZnCl_2$ complexes with bisazolylformazans have ultraviolet spectra resembling those of the hydrochlorides and sodium salts of the initial formazans (two maxima in close proximity in the spectrum).[155] This factor suggests that the structure of $ZnCl_2.L$ is analogous to that of the cyanine dyes (LIX).[147,155]

Hetarylformazans are ambident systems[179,180], containing several potential electron-donating centres: the nitrogen atoms of the formazans and azole rings and the O and S atoms of the benzothiazole and benzoxazole rings respectively. Therefore in the study of the molecular complexes (LXX) the problem of the location of the coordinate bond in the hetarylformazan system (competitive coordination) was solved[179]. In agreement with the results of quantum-chemical calculations[112], the infrared spectra[156] led to the conclusion that MX_n is coordinated to the $N_{(3)}$ atom of the azole fragment, and, in complexes having the composition $2TiCl_4.L$, to the $N_{(2\ or\ 4)}$ atom of the formazan ring[156].

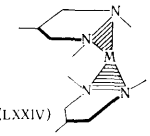
A square planar configuration is most characteristic of the chelate complexes of bivalent metals with the MN_4 coordination unit, to which the metal chelates of hetarylformazans also belong[148,152,181–184]. However, it has been shown for the chelate complexes of hetarylformazans[153,163,166–168,174,177,178] that the metal chelates with an MN_4 coordination unit can also have a non-planar structure: polymeric octahedral in the condensed phase and tetrahedral in solution.

In 1966 two independent investigations[163,174] showed that the nickel chelate complexes of *N*-azolylformazans are paramagnetic, in contrast to the analogous planar metal chelates of the aromatic series[10,88,185], and therefore have non-planar structures. The authors explained in different ways the appearance of paramagnetism in the nickel chelate complexes of formazans of the azole series: three

of the present authors[163] attributed it to a polymeric octahedral configuration of the complexes (MN_6) in the crystalline phase and a tetrahedral configuration (MN_4) in solutions; Pyl and Meyer[174] attributed it to an intramolecular octahedral configuration (LXXIII) containing the MN_4S_2 coordination unit.



(LXXIII)



(LXXIV)

In order to establish how general is the above change in the structure of the MN_4 coordination unit on passing from *N*-aryl to *N*-azolyl complexes in formazans, a study was made of the magnetic and polar properties of a large series of copper, nickel, and cobalt chelates of formazans of the azole series and the following observations were made:

(1) Nickel complexes of *N*-azolylformazans are of the high-spin type in both the crystalline phase and in solution regardless of the structure of the ligand (except for *o*-hydroxy- and carboxy-phenylformazan chelate complexes[164,165]).

(2) The cobalt chelate complexes of hetarylformazans are of the low-spin type, in the condensed phase, while in benzene and carbon tetrachloride solutions they are of the high-spin type.

(3) The copper, nickel, cobalt, and zinc chelate complexes in benzene, dioxan, and carbon tetrachloride solutions have polar structures with dipole moments in the range 1.7–2.5 D.

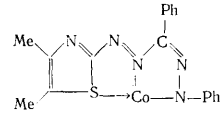
These data made it possible to ascribe a tetrahedral structure to metal chelates of hetarylformazans in solution, in agreement with the results of cryoscopic studies (the existence of the complexes as monomeric species in benzene and dioxan solutions)[153,163,167,177,178]. The polarity of the externally symmetrical (regardless of the type of polyhedron) chelate complexes of *NN*-diazolylformazans merits particular attention[153,167,168,177,178]. The polar model of a tetragonal pyramid with the metal atom above the plane of the metal-containing ring (cf. Garnovskii and coworkers[153,186]) conflicts with magnetochemical data. Therefore the most probable structure of the metal chelates of *NN'*-diazolylformazans, capable of explaining their magnetic and polar properties, we believe to be, by analogy with the complexes of other externally symmetrical *NN'*-disubstituted derivatives[187], the tetrahedral structure (LXXIV) with the metal-containing rings bent along the *N*–*N'* line at an angle α. This hypothesis is also supported by the finding that the nickel complexes of *NN'*-diarylformazans are paramagnetic in solution and have a dipole moment of 1.2 D.[177,178] The results (particularly for bivalent cobalt chelate complexes of hetarylformazans[167]) make it possible to reject the intramolecular octahedral structure (LXXIII) with M–N and M–S bonds.[174]

A polymeric octahedral configuration has been attributed to the metal chelates of formazans of heterocyclic series in the crystalline phase. It is consistent with the results of magnetochemical measurements and the high tendency of azoles to form intermolecular M–N bonds[152,153]. The explanation of the low-spin nature of the cobalt chelate complexes of hetarylformazans involves certain difficulties from this point of view[167,174,177]: their effective magnetic moments are of the order of 1.3–2 Bohr magnetons (B.M.) and can be attributed to the planar model, which is not inconsistent with theoretical and structural‡ considerations[185,188,189], or a spin-paired octahedron, which is comparatively rarely encountered. For this reason, X-ray diffraction data are necessary to reach a final conclusion about the structure of the chelate complexes of hetarylformazans in the crystalline phase. A preliminary report on the problem[190] still does not allow a definite conclusion.

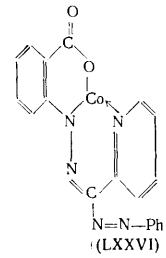
In contrast to the chelate complexes discussed above, the nickel chelates of *N*-(*o*-carboxyphenyl)-*N'* hetarylformazans (LXVIIIb)[164,165] as well as the analogous complexes of *o*-carboxyarylformazans[191–193] are diamagnetic (planar structure). The coordination saturation in complexes of this type [compounds (LXVIIIb)] probably involves the participation of the carbonyl oxygen. However, since there is reason to believe[192] that the chelates (LXVIIIb) have a structure in which the nickel is joined by a double bond, in this case too X-ray diffraction data will prove extremely useful. The metal chelates (LXIX) should probably also be planar[169].

The purely synthetic study by Seyhan[157,161,170–173], who first began to investigate 3-hetarylformazan complexes in 1954, stand alone from the standpoint of modern coordination chemistry. He did not employ any physical research techniques and therefore his structures of the complexes are open to serious objection. This applies particularly to the 2:1 metal chelates, to which the author attributes the structure of 1:1 complexes with an added ligand molecule[158,160,172,173].

In connection with the problem discussed above, the formulae of the cobalt complexes of hetarylformazans proposed by Pearse[194] [structure (LXXV)] and Beffa et al.[195] [structure (LXXVI)] are of very great interest:



(LXXV)



(LXXVI)

Whereas the first structure (LXXV) gives rise to doubts in connection with the possible involvement of the sulphur atom of the thiazole ring in coordination interaction[152,153,179], the second structure (LXXVI) appears to be fully justified.

Thus the introduction of the azole ring induces a preferential tetrahedral coordination of the chelate complexes of the formazan series (compared with the metal chelates of arylformazans) or leads to polymeric octahedral structures. Experimental results have shown[148,152,153,196,197] that both these effects are characteristic not only of metal chelates of the azole series with the MN_4 coordination unit, but also of MN_2O_2 and MN_2S_2.

The properties of the chelate complexes of hetarylformazans have been comparatively little investigated. There are isolated data on their stability[70,154,176] and their infrared spectra[70,122,156,164–166].

The dependence of the ν(C=N) shifts in the spectra of formazans on the structure of the ligand and the nature of the metal is a striking feature of the infrared spectroscopic data[166]. For formazans with the chelate structure, the transition from the chelate with a hydrogen-bond bridge

‡ By analogy with the structure of the nickel complexes of 3-methyl-1-phenyl-5-(*p*-tolyl)formazan[185].

to one of the inner complex type does not entail an appreciable change in the position of the band. On the other hand the ν(C=N) wavenumbers for the metal chelates of formazans with an open-chain structure are significantly reduced compared with the corresponding bands of the non-coordinated formazans[70,166]. The changes in the above infrared bands as a function of the metal are such that the shift $\Delta\nu$(C=N) is a maximum for the cobalt complexes.

In connection with the development of studies on the use of the complexes as ligands[179], the adducts of hetarylformazans with $CuCl_2$,[70,162] MCl_4,[156] and $Zn(OH)_2$[155] are of some interest. The number of MX_n molecules attached to the metal chelate of the hetarylformazan depends mainly on the nature of the metal and the ligand. Thus in the case of $CuCl_2$ it is determined by the number of azole rings[70,162] and in the case of MCl_4 (M = Sn or Ti) by the number of potential electron-donating centres (including the nitrogen atoms of the formazan ring)[153,156,179].

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The prospects for the further development of studies in the field of hetarylformazans are determined, apart from their theoretical interest (the problems of complex tautomeric equilibria, photochromic and thermochromic transformations, structure, colour, etc.), by the possibility of using them in various branches of science and engineering. In the introduction and in the description of the methods ofsynthesis, we already mentioned above certain practical applications. Now we shall emphasise particularly the use of tetrazolium salts obtained on the basis of formazans of the heterocyclic series as bioindicators. The tetrazolium salts derived from 1-hetarylformazans, which readily form complexes, are converted by enzymatic reduction into formazans forming deeply coloured complexes with the metal (cobalt) of the enzyme. The use of tetrazolium salts {particularly 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide[23,198]} in histochemistry for the determination of the activities of oxidation-reduction enzymes is based on this reaction[194].

Hetarylformazans and their derivatives are of considerable interest as dyes[3,5]. The azacyanines derived from benzothiazole[63], benzimidazole[141], and indazole[199,200] are dyes resembling the pentamethinecyanine dyes. The deeply coloured inner complexes of formazans containing OH and COOH groups have been patented by the Ciba[201] and Geigy[202,203] Companies as dyes for natural silk. Stable colours on cellulose fibres are produced by the copper complexes of formazans containing dichloropyrimidinyl substituents[204,205]. Hetarylformazans can be of interest as photochromic and thermochromic dyes[130,135] and also as pH indicators[70].

The study of the applications of hetarylformazans in analytical chemistry has been developing rapidly in recent years. Whereas in the series of arylformazans it is necessary to introduce additional groups into the formazan ring for this purpose (the SH group in dithizone[206], the hydroxy- and carboxy-groups in zincon[207], cyanoformazan-II,[208] etc.[5]), among 1-hetarylformazans capable of tautomerism there are extensive possibilities for the selection of effective analytical reagents.

The studies in the field are being carried out mainly by two groups of chemists: Japanese[44,45,209-213] and Soviet[214-220]. Spectrophotometric studies of the formation of bivalent nickel, copper, cobalt, zinc, and cadmium complexes with 1-hetaryl-3,5-diphenylformazans (hetaryl = thiazolyl, benzothiazolyl, selenazolyl, oxazolyl, and pyridyl) were described in reports by the first group. In the studies of the second group of investigators effective analytical reagents for copper, silver, nickel, zinc, lead, mercury, cadmium, and thallium were found among 1-benzazolyl- and 1,5-dibenzimidazolylformazans. The results concerning the application of 3-ethoxycarbonyl-1,5-di(tetrazol-2-yl)formazan as an excellent reagent for the colorimetric determination of copper and nickel[221] are also of interest.

All the foregoing considerations leave no doubt about the necessity for the intensification of research on hetarylformazans and their derivatives (particularly tetrazolium salts, verdazyl radicals, and complex compounds).

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Coordination Polymers with Inorganic Main Chains

S.V.Vinogradova and O.V.Vinogradova

A specific set of properties distinguishes coordination polymers with inorganic main chains. The review deals with modern ideas about the structures of these polymers, the possible ways of synthesising them, and a survey of the available data on the properties of metal-containing polymers such as polyphosphinates, polyarsinates, etc.
The bibliography includes 125 references

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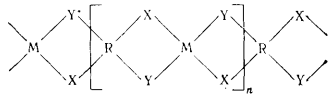
I. INTRODUCTION

Extensive experimental data have now accumulated on the synthesis and properties of polymeric organic derivatives of the elements and inorganic polymers. Polymers of this kind include in particular polyorganosiloxanes which have found numerous practical applications and also polyorganosiloxanes containing other elements, which possess a set of valuable properties [1]. Coordination polymers can also have main chains consisting of inorganic elements only. The available information about the synthesis and properties of coordination polymers has been described in a number of review publications [2-11].

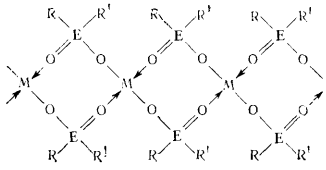
Coordination polymers can be divided into two types on the basis of the structure of the main chain.

1. Polymers with chains consisting of organic derivatives of the elements:



where M is a metal atom with a valence ≥ 2, X = −O−, −S−, =N−, etc., and Y = $>$CO, −N$<$, −N=O, $>$C=S, etc.

2. Polymers with inorganic chains:



where M is a metal atom, E the atom of an acid-forming element, for example phosphorus, arsenic, or sulphur, and R and R′ are organic groups.

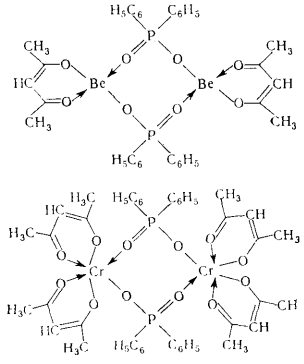
Coordination polymers of the second type, i.e. polymers with inorganic chains, appear to be the most promising. Some of them are fairly thermostable, are capable of flowing under load, and are soluble in the usual organic solvents.

The present review is devoted to coordination polymers with inorganic main chains. Polymers of this type, namely metal polyphosphinates, polyphosphinothioates, and polyarsinates, constitute an unusual group of coordination polymers with the ligands in bridge positions between the metal atoms. The chemistry of bridge coordination polymers has developed mainly during the last decade, although metal derivatives of phosphinic acids were known as early as 1896. [12]

One of the first experimental studies indicating the polymeric nature of the compounds of phosphinic acid with certain metals concerned the viscosity of the product synthesised by Healy and Kennedy [13] by the reaction of di-n-butylphosphinic acid with uranyl acetate, published in 1959. In 1962 Coates and Golightly [14] synthesised cobalt polyphosphinates. The reports of Block and coworkers on the polymeric nature of a number of metal phosphinates were published in the same year [15-18].

II. THE STRUCTURE OF COORDINATION POLYMERS WITH INORGANIC MAIN CHAINS

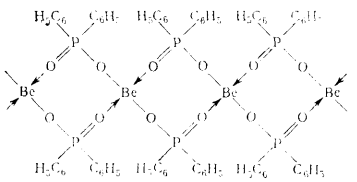
The hypothesis of the bridging properties of phosphinate anions, each of which is linked to two metal atoms, was already put forward in the first reports dealing with the synthesis of polyphosphinates. The bridge type of bond in beryllium and chromium polyphosphinate dimers was demonstrated by Block and coworkers [15,16,18] on the basis of an ebullioscopic determination of their molecular weights, infrared spectroscopic data, and microanalysis.



These dimers were obtained by the interaction of diphenylphosphinic acid with an excess of beryllium acetylacetonate *in vacuo* at 100°C and with an excess of chromium acetylacetonate at 240°C. [15,18] Subsequently the structure of the

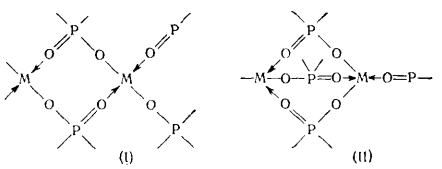
chromium phosphinate dimer was confirmed by an X-ray diffraction study of its single crystals[19]. In these cyclic derivatives the metal atoms are incorporated in the chelate ring with acetylacetone and simultaneously in an eight membered coordination ring with the phosphinate groups[20].

In those cases where diphenylphosphinic acid was introduced into the reaction with beryllium acetylacetonate in a twofold molar excess, the acetylacetonate groups were completely split off and the product was a polycyclic polymer with phosphinate bridges, having the following structure according to the authors[19]:



Block proposed a similar structure also for the polyphosphinates of other metals: cobalt and zinc[16,21-27] and chromium[15,28-34].

Later the Italian investigators Ripamonti, Giancotti, Giordano, and others[35-42] established by X-ray diffraction that certain polyphosphinates of the type MX_2 (M is a bivalent metal and X the phosphinate anion) have a structure different from structure (I) proposed by Block. Their X-ray diffraction study of zinc polydi-n-alkylphosphinates and poly-n-butylphenylphosphinate showed that the chain structure in these crystalline polymers corresponds to structure (II), which includes alternating single and triple bridges:



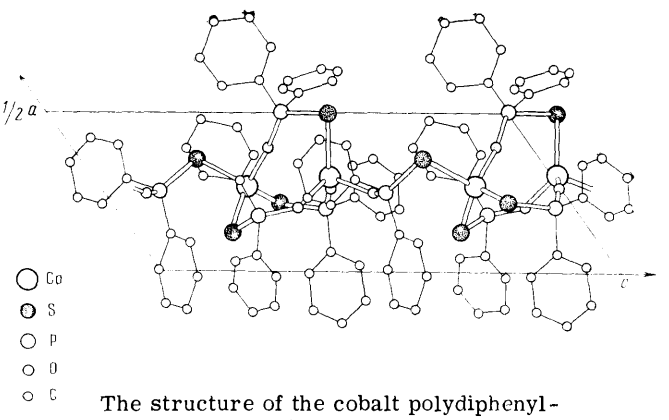
(I) (II)

According to the authors, this structure provides the best explanation of the elastic properties of the amorphous metal polyphosphinates at low temperatures, estimated from the brittleness temperatures[22], since polymeric chains with a type (II) structure should be fairly elastic owing to the possibility of rotation about the P–O and O–M single bridge bonds[35,38,39]. X-Ray diffraction data for cobalt polydi-n-alkylphosphinates[35,38,39] and mixed zinc-containing polymers based on di-n-butyl- and diphenyl-phosphinic acids with the general formula $\{Zn[(C_4H_9)_2PO_2]_{2-2x}[(C_6H_5)_2PO_2]_{2x}\}_n$[39,40] also support structure (II).

Giordano et al.[40] concluded on the basis of an X-ray diffraction study of zinc poly-n-butylphenylphosphinate that the phenyl and n-butyl side groups of the phosphorus atoms in the polymer chain are distributed in a non-ordered fashion.

The influence of the nature of the side groups at the phosphorus atom on the conformation of the polyphosphinate macromolecules has been investigated[37] for mixed beryllium polyphosphinates incorporating di-n-butyl- and diphenyl-phosphinate anions as bridging ligands. It was shown that the skeletal structure of beryllium polydiphenylphosphinate and of mixed polymers with a high content of diphenylphosphinate groups differs from the structure of beryllium polymers in which di-n-butylphosphinate groups predominate. It was found that, depending on the nature of the organic groups, the macromolecule can have a helical or extended conformation, the former being probably characteristic of diphenylphosphinate polymers and the latter of di-n-alkylphosphinate polymers. It is believed that, when a critical content of the more bulky diphenylphosphinate group is reached in the mixed polymer, the extended chain conformation becomes energetically less favourable owing to the appearance of a steric factor, which leads to the generation of a helical structure of the mixed polymers.

X-Ray diffraction was also used by Bruckner et al.[43] to investigate the structure of cobalt polydiphenylphosphinomonothioate (see Figure). The Figure shows that the structure of the monoclinic crystals of this polymer contains two types of cobalt atoms, those of one type being linked to one sulphur atom and three oxygen atoms and those of the other type to three sulphur atoms and one oxygen atom, i.e. the structure is analogous to structure (II) of metal polyphosphinates.



The structure of the cobalt polydiphenylphosphinomonothioate chain.

Thus the distribution of phosphinate groups in the bridge positions between the metal atoms in the polymer chain may be regarded as established for metal polyphosphinates and related polymers. As mentioned above, the structure of the polymer chain of metal-containing polymers based on phosphinic acids can be described in terms of two main structures: (I) and (II), differing in the distribution of the phosphinate groups between the metal atoms. However, one should note that data favouring structure (II) have been obtained only for bivalent metal polyphosphinates with a coordination number of four. Furthermore, they are based on a study of the structure of single crystals grown under special conditions.

The polyphosphinate single crystals were obtained on slow evaporation of the solvent from the polymer solution in water[44] or in a benzene–alcohol mixture[39,40]. Block[45] noted that structure (II) is in principle impossible for certain polyphosphinates, for example for the *trans*-form of chromium polydiphosphinate having the general formula $|Cr(H_2O)(OH)(OPRR'O)_2|_n$.

It follows from the foregoing that it is as yet impossible to reach an unambiguous conclusion about the distribution of the phosphinate bridge groups in the polymers. It is probably also impossible to rule out the possibility of a structure of the polyphosphinates in which the polymer chain includes units of two types corresponding to structures (I) and (II).

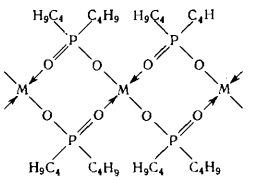
In the treatment below we shall employ the structural formulae of the coordination polymers with inorganic main chains which were proposed by the authors of the studies quoted.

III. SYNTHESIS OF METAL POLYPHOSPHINATES BY THE POLYCOORDINATION REACTION

Metal polyphosphinates have been reviewed by Block[45] and in separate chapters in a number of monographs[46-50]. They can be obtained by the reaction of diorganophosphinic acids with metal salts, by the oxidative decarbonylation of metal carbonyls, by the pyrolysis of complex metal salts with phosphinic acids, and by other methods.

Metal polyphosphinates are usually obtained by the polycoordination of diorganophosphinic acids and various metal-containing compounds: chlorides, acetates, nitrates, acetylacetonates, carbonyls, and organometallic derivatives. The Table shows that the metal polyphosphinates described in the literature differ appreciably in their polymerisation coefficients.

The polycoordination of phosphinic acids with metal salts can be achieved in solution[18,22,23,41,56-58,61,64,65-69,75], in the melt[16,18,51,65,75], and at an interface[16,35,41,44,54]. Thus zinc, cobalt, and manganese polydibutylphosphinates were obtained from the corresponding metal salts and di-n-butylphosphinic acid or its sodium salt by polycoordination in solution and at an interface[41,69]:



where M = Zn, Co, or Mn.

The interaction of phosphinic acids with metal salts is a polycondensation process. The formation of metal-containing coordination polymers by the polycoordination method has a number of characteristic features due to the nature of the M–O bonds arising in this process: ionic–covalent and coordinate.

The polycoordination reactions of phosphinic acids with metal salts proceed readily even at the usual temperatures. However, the ease of formation of coordination compounds

Metal polyphosphinates and their properties.

No.	Repeat unit	Degree of polymerisation	Polymer solvent	[η], dl g^{-1}	M.p., °C	Temperature of the onset of weight loss, °C		References
						in air	in an inert atmosphere	
1	2	3	4	5	6	7	8	9
1	Be[OP(CH$_3$)$_2$O]$_2$				465	522[a]	540[a]	13, 18, 51, 52
2	Be[OP(C$_4$H$_9$)$_2$O]$_2$	138; 37	Benzene, CHCl$_3$, CCl$_4$	0.42[b] (benzene)	452	—	410[a] 515[a]	37, 51, 53
3	Be[OP(C$_6$H$_{11}$)$_2$O]$_2$	62; 215	Hydrocarbons, CCl$_4$			457[a]	445[a]	51, 53
4	Be[OP(C$_7$H$_{15}$)$_2$O]$_2$	32; 140	Hydrocarbons				420[a]	51, 53
5	Be[OP(CH$_3$)(C$_6$H$_5$)O]$_2$	94; 15	Benzene		infusible	500[a]	525[a]	51, 53
6	Be[OP(C$_6$H$_5$)$_2$O]$_2$		—		infusible	545[a]	530, 610[a]	16,18,37,51,52,54
7	Be[OP(C$_6$F$_5$)$_2$O]$_2$		—		infusible		470[a]	51
8	Be[OP(CF$_3$)(C$_6$H$_5$)O]$_2$	30; 157	Toluene					53, 55
9	Be[OP(CH$_3$)$_4$O]$_2$		—				515[a]	51
10	Zn[OP(CH$_3$)$_2$O]$_2$		Water		340		440	23, 39, 54
11	Zn[OP(C$_4$H$_9$)$_2$O]$_2$	>25; 56	Benzene, CHCl$_3$, CCl$_4$	0.3–0.7[b] 5.45[b] (benzene), CHCl$_3$)	177, 250	185, 200	250	21, 22, 24, 35, 38, 39, 44, 56, 57
12	Zn[OP(C$_6$H$_{13}$)$_2$O]$_2$		Non-polar solvents		152			38
13	Zn[OP(C$_7$H$_{15}$)$_2$O]$_2$	200	Benzene, toluene, CHCl$_3$	18.5[b] (benzene), CHCl$_3$)	140	170		57
14	Zn[OP(C$_8$H$_{17}$)$_2$O]$_2$		Benzene, toluene, CHCl$_3$, CCl$_4$	5.22[b] (benzene),	150–160	170		57, 58
15	Zn[OP(C$_9$H$_{19}$)$_2$O]$_2$		Benzene, toluene, CHCl$_3$, CCl$_4$	0.25[b] (benzene)	150–160	170		57
16	Zn[OP(C$_{10}$H$_{21}$)$_2$O]$_2$		Non-polar solvents		151			38
17	Zn[OP(C$_{12}$H$_{25}$)$_2$O]$_2$		Benzene, toluene CHCl$_3$, CCl$_4$	0.15[b] (benzene)		170		57
18	Zn[OP(C$_4$H$_9$)$_2$O][OP(C$_6$H$_{13}$)$_2$O]		Benzene, toluene, CHCl$_3$, CCl$_4$	0.4[b] (benzene)	150			38
19	Zn[OP(C$_4$H$_9$)$_2$O][OP(C$_7$H$_{15}$)$_2$O]		Benzene, toluene, CHCl$_3$, ether		155–165	180		59
20	Zn[OP(C$_4$H$_9$)$_2$O][OP(C$_8$H$_{17}$)$_2$O]	>20	Chloroform	0.4–0.5 (benzene, CHCl$_3$)	120, 150			22, 54
21	Zn[OP(C$_4$H$_9$)$_2$O][OP(C$_{10}$H$_{21}$)$_2$O]		Benzene, CHCl$_3$, CCl$_4$					38
22	Zn[OP(cyclo-C$_6$H$_{11}$)$_2$O]$_2$		—		360–380	170		59
23	Zn[OP(CH$_3$)(C$_6$H$_5$)O]$_2$	>30	Benzene, CHCl$_3$, H$_2$O	0.02 (CHCl$_3$)	200		415, 425	16, 23, 39, 54, 60
24	Zn[OP(CH$_3$)$_2$O][OP(C$_6$H$_5$)$_2$O]	7	Benzene, CHCl$_3$		120		430	23, 24, 39, 54
25	Zn[OP(CH$_3$)(C$_6$H$_5$)O][OP(C$_6$H$_5$)$_2$O]	>25	Benzene CHCl$_3$	0.02 (CHCl$_3$)	150		430	24
26	Zn[OP(C$_4$H$_9$)$_2$O][OP(C$_6$H$_5$)$_2$O]		Benzene, CHCl$_3$, ethanol	0.53[b] (benzene)		200		56
27	Zn[OP(C$_4$H$_9$)$_2$O][OP(CH$_3$–C$_6$H$_3$–O–C$_6$H$_3$–CH$_3$)O]		Ethanol, benzene, CHCl3	0.81[b] (benzene)			195	56
28	Zn[OP(C$_4$H$_9$)]O][OP(CH=CHC$_6$H$_4$)O]		CHCl$_3$	0.13[b] (CHCl$_3$)				56
29	Zn[OP(CH=CHC$_6$H$_4$)$_2$O]		Sovol		340–360	285, 170	335	56, 61, 59
30	Zn[OP(CH$_3$–C$_6$H$_3$–O–C$_6$H$_3$–CH$_3$)O]$_2$		—	—	450	465		56
31	Zn[OP(C$_6$H$_5$)$_2$O]$_2$			—	—	425	450, 495, 460	16, 23, 39, 54, 56, 59, 62
32	Co[OP(CH$_3$)$_2$O]$_2$		Water		342–343		445	14, 24
33	Co[OP(C$_2$H$_5$)$_2$O]$_2$	9	Benzene			285[a], 310[a]		59
34	Co[OP(C$_4$H$_9$)$_2$O]$_2$	20	Benzene, CCl$_4$, water			295, 330[a]		35, 44, 63, 64

Table (cont'd)

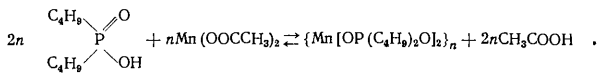
No.	Repeat unit	Degree of polymerisation	Polymer solvent	[η], dl g^{-1}	M.p., °C	Temperature of the onset of weight loss, °C		References
						in air	in an inert atmosphere	
1	2	3	4	5	6	7	8	9
35	Co [OP(CH$_3$) (C$_6$H$_5$)O]$_2$	>30	Benzene, $CHCl_3$, water	0.02—0.05	275			
		13		($CHCl_3$)	226—227		445	14, 24
36	Co [OP(C$_6$H$_5$)O]$_2$		Benzene, water		infusible		485	14, 24, 54, 65
37	Co [OP(CH$_3$)$_2$O] [OP(C$_6$H$_5$)$_2$O]	14	$CHCl_3$		275			14, 24
38	Co [OP(CH$_3$)(C$_6$H$_5$)O] [OP(C$_6$H$_5$)$_2$O]	8	$CHCl_3$		140			24
39	Co[OP(CH$_3$C$_6$H$_3$—O—C$_6$H$_3$—CH$_3$)O]$_2$					360, 450[a]		65
40	Mo [OP(C$_6$H$_5$)$_2$O]$_2$		THF, $CHCl_3$, DMF		230—235	200		66, 67, 68
41	W [OP(C$_6$H$_5$)$_2$O]$_2$				300	340	390	66, 67, 68
42	UO_2[OP(C$_2$H$_5$)$_2$O]$_2$	14	Benzene			260, 380[a]		63
43	UO_2[OP(C$_4$H$_9$)$_2$O]$_2$	11	Benzene			300, 420[a]		63
44	UO_2[OP(C$_6$H$_5$)$_2$O]$_2$	9	Benzene			395, 460		58, 63
45	Mn [OP(C$_4$H$_9$)$_2$O]$_2$		Benzene, toluene	0.87[b] (benzene)	220	230		57, 69
46	Mn [OP(C$_7$H$_{15}$)$_2$O]$_2$		Benzene, toluene	0.80[b] (benzene)	200	225		57
47	Mn [OP(C$_8$H$_{17}$)$_2$O]$_2$	25	Benzene, toluene	0.60[b] (benzene)	215	200		57, 58
48	Mn [OP(C$_9$H$_{19}$)$_2$O]$_2$		Benzene, toluene, $CHCl_3$	0.45[b] (benzene)	190	170		57
49	Mn [OP(C$_{12}$H$_{25}$)$_2$O]$_2$		Benzene, toluene, $CHCl_3$	0.13[b] (benzene)	89—93	170		57
50	Mn [OP(*trans*-C$_6$H$_{11}$)$_2$O]$_2$		Insoluble		—	230		59
51	Mn [OP(C$_6$H$_5$)$_2$O]$_2$		Insoluble		440	450	470	66, 67, 68
52	Mn [OP(C$_4$H$_9$)$_2$O]$_3$		Insoluble		—	180		69
53	Al(OC$_3$H$_7$)$_2$[OP(CH$_3$)$_2$O]	3	Aromatic hydrocarbons, alcohols, ethers					70
54	Al [OP(CH$_3$)$_2$O]$_3$		—	—	infusible		495[a]	71
55	Al [OP(CH$_2$CH$_2$CF$_3$)$_2$O]$_3$		—	—	355		120, 370[a]	71
56	Al [OP(C$_5$H$_{11}$)$_2$O]$_3$	—	—		390—415			71
57	Al [OP(C$_6$H$_{13}$)$_2$O]$_3$	—	—	—	380—410			71
58	Al [OP(C$_8$H$_{17}$)$_2$O]$_3$	—	THF		385—415			71
59	Al [OP(C$_5$H$_{11}$)$_2$O][OP(C$_7$H$_{15}$)$_2$O]$_2$	—	THF		335 (400)			71
60	Al[OP(C$_6$H$_{13}$)$_2$O]$_{1.5}$[OP(C$_8$H$_{17}$)$_2$O]$_{1.5}$		THF		300—310		170, 425[a]	71
61	Al [OP(C$_7$H$_{15}$)$_2$O] [OP(C$_4$H$_9$)· ·(C$_6$H$_5$CH$_2$)O]$_2$	270—670	THF, toluene, heptane	10—30 (THF)	285—300		170, 400[a]	71
62	Al [OP(C$_8$H$_{17}$)$_2$O] [OP(C$_4$H$_9$)· ·(C$_6$H$_5$CH$_2$)O]$_2$	23—1050	THF, toluene, heptane	15—37 (THF)	300—320		170, 380[a]	71
63	Al [OP(C$_8$H$_{17}$)$_2$O]$_{1.5}$[OP(C$_{18}$H$_{37}$)$_2$O]$_{1.5}$	12—29	THF	8—31 (THF)	330—370	170, 315[a]		71
64	Al[OP(C$_4$H$_9$)(C$_7$H$_7$)O]$_2$[OP(C$_7$H$_{15}$)$_2$O]	700	THF	35 (THF)	295		400	72
65	Al [OP(C$_4$H$_9$)(C$_7$H$_7$)O]$_2$[OP(C$_8$H$_{17}$)$_2$O]	560	THF	37 (THF)	315		400	72
66	Al [OP(C$_6$H$_5$)$_2$O]$_3$		—	—	infusible	480[a]		73
67	Al(F) [OP(CH$_3$)$_2$O]$_2$		—	—	385—430		500	74, 75
68	Al(F) [OP(C$_5$H$_{11}$)$_2$O]$_2$		—		250—260		350	74
69	Al(F) [OP(C$_6$H$_{13}$)$_2$O]$_2$	140	THF		185—230		350	74
70	Al(F) [OP(C$_8$H$_{17}$)$_2$O]$_2$		THF		200—220		350	74
71	Al(F)[OP(C$_6$H$_{13}$)$_2$O][OP(C$_8$H$_{17}$)$_2$O]		THF		110—130		350	74
72	Al(F)[OP(C$_7$H$_{15}$)$_2$O][OP(C$_{12}$H$_{25}$)$_2$O]		THF		70—85		350	74
73	Al(F)[OP(C$_6$H$_5$)$_2$O]$_2$				420—450		500	74
74	Al(Cl)[OP(C$_6$H$_{13}$)$_2$O]$_2$	6	THF					74
75	Fe(AcAc)[OP(C$_6$H$_5$)$_2$O]$_2$	15	$CHCl_3$, ethanol, benzene				340	75
76	Fe(CO)[OP(C$_6$H$_5$)$_2$O]$_3$					90		66, 67
77	Fe(CO)$_2$[OP(C$_7$H$_5$)$_2$O]$_2$		Benzene				300	76
78	Fe [OP(C$_6$H$_5$)$_2$O]$_3$						300	67
79	Zr [OP(C$_6$H$_5$)$_2$O]$_3$		Organic solvents			455[a]		73, 77
80	Cr(H$_2$O)(OH) [OP(CH$_3$)$_2$O]$_2$	>60	$CHCl_3$, water	0.13 ($CHCl_3$)		350		30, 32
81	Cr(H$_2$O)(OH) [OP(C$_8$H$_{17}$)$_2$O]$_2$		$CHCl_3$	0.30—0.67 ($CHCl_3$)				21, 78, 79
82	Cr(H$_2$O)(OH) [OP(CH$_3$)(C$_6$H$_5$)O]$_2$	>25	$CHCl_3$	0.1—0.78 ($CHCl_3$)	infusible		365	30, 32, 54, 78—82
83	Cr(H$_2$O)(OH [OP(C$_6$H$_5$)$_2$O]$_2$	345	Benzene, $CHCl_3$, THF	0.04—1.0 ($CHCl_3$)		355	375	28, 30, 32, 34, 78, 79, 82, 83
84	Cr(OH) [OP(C$_8$H$_{17}$)$_2$O]$_2$		Ethanol					78
85	Cr(OH) [OP(CH$_3$)(C$_6$H$_5$)O]$_2$		Ethanol					78
86	Cr(OH) [OP(C$_6$H$_5$)$_2$O]$_2$		$CHCl_3$	0.12—1.0 ($CHCl_3$)				78
87	Cr(OH)[OP(C$_6$H$_5$)$_2$OH][OP(C$_6$H$_5$)$_2$O]$_2$	26						84
88	Cr(CO) [OP(C$_6$H$_5$)$_2$O]$_3$	10	Ethanol, benzene		340	200		67, 76
89	Cr [OP(CH$_3$)$_2$O] [OP(CH$_3$)(C$_6$H$_5$)O]$_2$		—	—		200	490 155	33, 82, 85, 86
90	Cr [OP(CH$_3$)(C$_6$H$_5$)O]$_2$[OP(C$_8$H$_{17}$)$_2$O]						~400	87
91	Cr [OP(C$_6$H$_5$)$_2$O]$_3$		—	—		320		86
92	Cr(AcAc) [OP(C$_6$H$_5$)$_2$O]$_2$	19	Benzene, $CHCl_3$			300[a]	336	15, 88—91
93	Cr(AcAc) [OP(C$_6$H$_5$)$_2$O] [OP(CH$_3$· ·C$_6$H$_3$OC$_6$H$_3$CH$_3$)O]	16	Benzene, $CHCl_3$			150, 320[a]		88
94	TiO [OP(CH$_3$)$_2$O]$_2$	34	Organic solvents		230—250		450	92, 93
95	TiO [OP(CH$_3$)(C$_6$H$_5$)O]$_2$	18	Benzene, $CHCl_3$	0.06—0.14 ($CHCl_3$)	280		435	93
96	TiO [OP(C$_6$H$_5$)$_2$O]$_2$	>20	Benzene, $CHCl_3$	0.06—0.14 ($CHCl_3$)	300		450	93—96
97	TiCl$_2$[OP(C$_8$H$_5$)O]$_2$	>20	Benzene, $CHCl_3$	0.03 ($CHCl_3$)	300		370	93
98	Ti(OC$_4$H$_9$)$_2$[OP(CH$_3$)$_2$O]$_2$	5						93, 97, 98
99	Ti [OP(C$_6$H$_5$)$_2$O]$_4$		$CHCl_3$, ethanol, DMF, chlorobenzene		135	350[a]	200	73, 99

[a] The temperature corresponding to the decrease of the weight of the polymer by 10%.
[b] Intrinsic viscosity. [All the figures in this column appear to be intrinsic viscosities (Ed. of Translation)].

does not always ensure the formation of polymers with high molecular weights, since chain growth is frequently arrested at the stage involving the formation of low-molecular-weight or oligomeric compounds.

In order to find the optimum conditions for the synthesis of various metal polyphosphinates and other coordination polymers with inorganic main chains, Korshak and coworkers [69] investigated the characteristics of this process. They chose for investigation the polycoordination of di-n-butylphosphinic acid with manganese acetate under different conditions. The resulting coordination polymer—manganese polydi-n-butylphosphinate—is comparatively readily soluble in hydrocarbon solvents, which permits the determination of the viscosity of its solutions.

A study was made of the influence on the yield and intrinsic viscosity of the resulting manganese polydi-n-butylphosphinate of factors such as the nature of the reaction medium, the temperature and duration of the reaction, reactant concentration, and reactant ratio. It was found that the acetic acid liberated in the reaction degrades the manganese polydi-n-butylphosphinate formed under the conditions of the synthesis of the coordination polymer; consequently the polycoordination of phosphinic acid with manganese acetate must be regarded as a reversible polycondensation process:



Polymers with the highest molecular weights were obtained in a high-boiling solvent (Dinil) at about 140°C *in vacuo* (30 mmHg) in a stream of an inert gas.

Korshak and coworkers [57,69] showed that the interaction of di-n-butylphosphinic and other phosphinic acids with metal acetates takes place even when a powdered mixture of the two components is ground at room temperature. The amount of acetic acid liberated under these conditions during 10–15 min grinding of the starting materials in a thin layer is 70–80% of theoretical. Owing to the large surface area of the powdered mixture, acetic acid is very rapidly removed from reaction sphere as a result of its volatility. Subsequent treatment of the reaction mass with ethanol leads to the formation of a polymer with a high molecular weight.

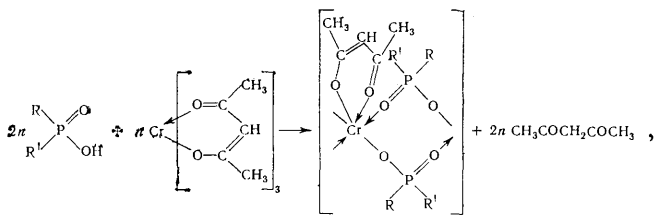
When the reaction is carried out in two stages, in the solid phase and in ethanol, the polymer with the maximum molecular weight is formed from di-n-butylphosphinic acid and manganese acetate taken in various proportions when stoichiometric amounts of the components interact [69], as in the single-stage polycoordination in solution. Thus, as in many other instances of polycondensation, in the formation of a coordination polymer with bridge ligands the rule of the non-equivalence of functional groups operates [101].

Korshak, Vinogradova, and coworkers [57,69,102] synthesised manganese and zinc polyphosphinates based on diphenyl-, dicyclohexyl-, distyryl-, di-n-butyl-, di-n-heptyl-, di-n-octyl-, di-n-nonyl-, and other phosphinic acids by the polycoordination of the acids with metal acetates and acetylacetonates. The molecular weights of manganese polydi-n-octylphosphinate with an intrinsic viscosity $[\eta] = 0.60$ dl g^{-1} (benzene, 50°C, $c = 1$ g dl^{-1}) and zinc polydi-n-butylphosphinate with $[\eta] = 5.45$ dl g^{-1} (benzene, 25°C, $c = 1$ g dl^{-1}), determined ebullioscopically in benzene, proved to be 8000 and 18 000 respectively. The molecular weight of zinc polydi-n-heptylphosphinate with $[\eta] = 18.50$ dl g^{-1} (benzene, 25°C, $c = 1$ g dl^{-1}), determined by the light scattering method in toluene, amounted to 74 000.

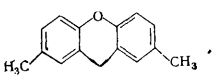
The interaction of phenylmethylphosphinic acid with zinc acetate in ethanol, leading to the formation of zinc polyphenylmethylphosphinate $\{Zn[OP(C_6H_5)(CH_3)O]_2\}_n$ with a molecular weight of 5600 has been described [16,54].

Slota et al. [51] synthesised a number of polymers of beryllium diorganophosphinates by the reaction of stoichiometric amounts of beryllium acetylacetonate with dimethyl-, 1,4-tetramethylene-, phenylmethyl, diphenyl-, and other phosphinic acids. The reaction was carried out in the melt, initially in an inert gas stream at 130°C and then *in vacuo* at 200°C. The resulting beryllium-containing polymers based on phenylmethyl-, di-n-butyl-, and di-n-pentyl-phosphinic acids had molecular weights of 30 000, 50 000, and 26 000 respectively.

Block and coworkers [30–34,78,86] and other investigators [79,87,88,90,103,104] made a detailed study of the synthesis of chromium-containing polyphosphinates. The polymer with tervalent octahedral chromium atoms is formed when a mixture of the monomeric chelate (chromium acetylacetonate) and substituted phosphinic acids is heated in the range 170–250°C in the melt or in a high-boiling solvent in an inert gas atmosphere via the mechanism



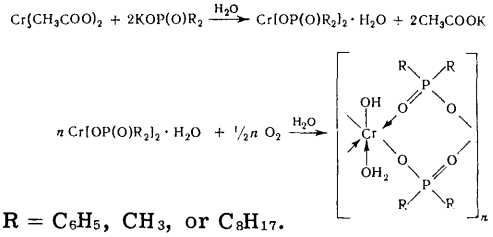
where R = C_6H_5 and R′ = C_6H_5, CH_3, or



The molecular weight of the benzene-soluble fraction of this polymer was about 10 000. [88–91]

The acetylacetonate group present in chromium polydiphenyl phosphinate as an additional chelating ligand can be replaced by another bidentate ligand, for example picolinic acid, as a result of exchange reactions occurring at elevated temperatures [89,91].

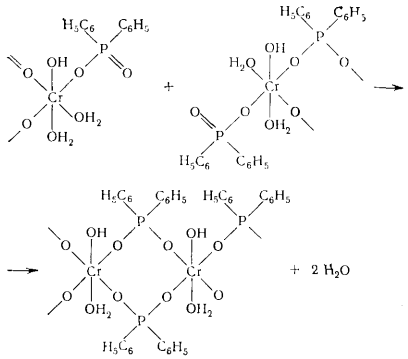
The examination of the structures of chromium polyphosphinates in terms of molecular models [105] showed that, when the dimensions of the additional ligand at the metal atom are greater than those of the acetylacetonate ligand, an appreciable steric hindrance arises in the chain and prevents the formation of high-molecular-weight polymers. For this reason, further studies were directed to the synthesis of chromium polydiphenylphosphinates with small additional ligands at the metal atom, such as water molecules and hydroxy-groups [30,32,78–83], instead of organic bidentate ligands. In particular, Block and coworkers [30,32,34] developed a method for the preparation of a polymer by the oxidation of the chromium(II) phosphinate complex in accordance with the mechanism



where R = C_6H_5, CH_3, or C_8H_{17}.

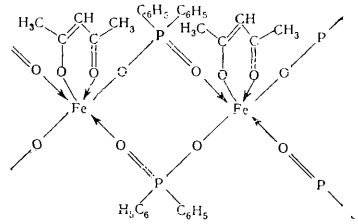
The oxidation of the insoluble intermediate chromium-(II) complex $Cr[OP(C_2H_5)_2O]_2.nH_2O$ was achieved by mixing in air its suspension in a water–tetrahydrofuran (THF) mixture for 12 h. The resulting oligomer with five or six repeating chain units $\{[\eta] = 0.03-0.04$ dl g^{-1} in chloroform$\}$ is readily soluble in benzene, chloroform, THF, and dioxan. On heating solutions of such oligomers in chloroform at 55°C for about 100 h, polymer chains with polymerisation coefficients up to 345 and intrinsic viscosities in chloroform $[\eta] = 0.7-1.0$ dl g^{-1} are formed.

The high-molecular-weight polymer is probably formed as a result of the interaction of the terminal groups of the oligomers with elimination of the water coordinated to the metal, via the mechanism



When other oxidants are used, ligands such as the nitro- and nitroso-groups can be introduced into the polymer chain instead of the hydroxide ion [80]. Additional treatment of the polymer $[Cr(H_2O)(OH)(OPR_2O)_2]_n$ with one mole of phosphinic acid per unit leads to the formation of chromium polytriphosphinates, i.e. in these polymers the additional ligands at the metal atom are the phosphinate anions which function as bridges in the main chain [33,82,85]. After the introduction of the third phosphinate group per chromium atom in the chain, the polymer ceases to be fusible and soluble.

The interaction of iron(III) acetylacetonate with diphenylphosphinic acid in solution, in the melt, or at an interface at 80–108°C led to the formation of iron(III) polydiphenylphosphinate [75]:

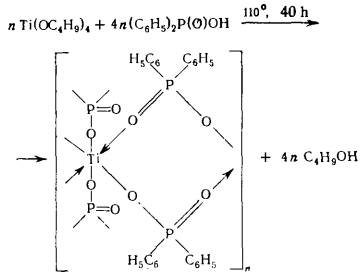


The resulting polymer was divided into four fractions, the first of which consisted of the dimer, the second and third of linear polymers with molecular weights of 4000 and 8800 respectively, and the fourth was insoluble.

Flagg and Schmidt [71,72,74,75,106–108] synthesised coordination polymers with Al–O–P linkages in the main inorganic chain. Aluminium-containing coordination polymers with the general formula $[Al(OPRR'O)_3]_n$ are usually obtained from triethylaluminium or the ether adduct of tetrahydroaluminate and the corresponding phosphinic acids via the mechanism

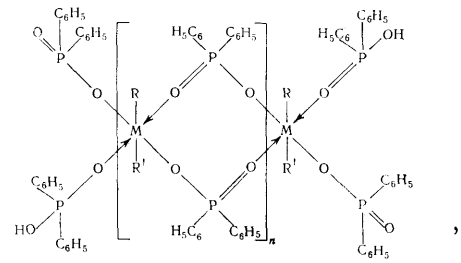
$$3nR_2P(O)OH + nR'_3Al \xrightarrow{THF,\ -70^\circ} \{Al[OPR_2O]_3\}_n + 3nR'H$$

Sutton and Wood [73] described the synthesis of a titanium-containing polymer by the interaction of tetrabutoxytitanate with diphenylphosphinic acid in toluene:



IV. SYNTHESIS BY THE OXIDATIVE DECARBONYLATION OF METAL CARBONYLS

Podall and Japalucci [76,84] proposed the oxidative decarbonylation of metal carbonyls for the synthesis of metal polyphosphinates. As a result of the oxidation-reduction reactions occurring under the influence of ultraviolet irradiation, they obtained polymers with the following tentative structure from chromium hexacarbonyl, iron pentacarbonyl, and diphenylphosphinic acid:



where R = R′ = CO for M = Fe and R = CO and R′ = $-O-\underset{\displaystyle H_5C_6\quad C_6H_5}{\overset{\displaystyle\quad\ \ |}{P}}-O-$ for M = Cr.

Iron polydiphenylphosphinate proved to be insoluble, but fractions soluble in benzene and chloroform were isolated from chromium polydiphenylphosphinate. The minimum molecular weight of these fractions corresponded to the dimer and the maximum molecular weight was 7130.

Iron-containing metal polyphosphinates were obtained from iron nonacarbonyl in a much higher yield than from the pentacarbonyl, the reaction occurring in the absence of ultraviolet irradiation [68]. The corresponding metal-containing polymers were also obtained from manganese, tungsten, and molybdenum carbonyls [66–69].

The study by Korshak, Vinogradova, and coworkers [69] on the oxidative decarbonylation of manganese decacarbonyl with di-n-butylphosphinic acid under different conditions showed that manganese polydi-n-butylphosphinate with the maximum intrinsic viscosity $\{[\eta] = 1.13$ dl g^{-1}, benzene, 70°C, $c = 1$ g $dl^{-1}\}$ was obtained when the process was carried out in benzene under ultraviolet irradiation. The reaction proceeds via the mechanism

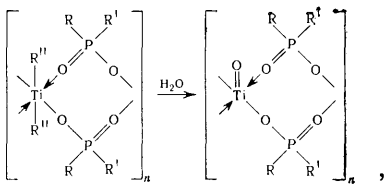
$$4n(C_4H_9)_2\overset{\displaystyle O}{\underset{\displaystyle OH}{P}} + nMn_2(CO)_{10} \xrightarrow{h\nu} \{[(C_4H_9)_2PO_2]_2Mn\}_n + 10nCO + 2nH_2$$

Other Methods for the Synthesis of Polyphosphinates

Dahl and Block [93] described the preparation of a coordination polymer of titanium (with $n = 18$) by the pyrolysis of the complex of titanium tetrachloride with diethyl diphenylphosphinate:

$$n\,TiCl_4 \cdot [OP(C_6H_5)_2OC_2H_5]_2 \xrightarrow{\Delta} \{TiCl_2[OP(C_6H_5)_2O]\}_n + 2nC_2H_5Cl\ .$$

It was shown that titanium polyphosphinates with a higher molecular weight can be obtained by the hydrolysis of dichloro- or dialkoxy- titanium polyphosphinates via the mechanism



where R and R′ = C_6H_5 and R″ = Cl or OC_4H_9.

Synthesis of Mixed Metal Polyphosphinates

The synthesis of mixed metal polyphosphinates by the interaction of two different phosphinic acids with metal-containing compounds under conditions analogous to those in the synthesis of homopolymers has been described [22-24, 38,39,54,56,59,71].

Thus mixed polyphosphinates with molecular weights up to 10 000 were synthesised by the joint polycoordination of two phosphinic acids with zinc, cobalt, and beryllium chlorides, acetates, and acetylacetonates [23,24,37-39,54].

Flagg and Schmidt [71] synthesised a large group of mixed high-molecular-weight aluminium polyphosphinates by the reaction of aluminium hydride or ethoxide with phosphinic acids of different structure in THF solution at −70°C. Thus the aluminium-containing polyphosphinates

$$\{[(C_4H_9)(C_6H_5CH_2)PO_2]_2Al[O_2P(C_8H_{17})_2]\}_n$$

and $\{[(C_4H_9)(C_6H_5CH_2)PO_2]_2Al(O_2P(C_7H_{15})]_2\}_n$

are soluble polymers with anomalously high intrinsic viscosities (up to 37 dl g^{-1}, 25°C, THF) and molecular weights of $(20-78) \times 10^4$.

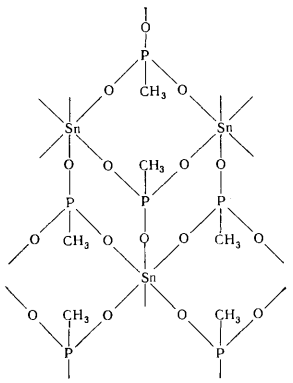
Korshak et al. [88] synthesised chromium-containing mixed polyphosphinates based on diphenyl- and 2,2′-(4,4′-dimethyl-1,1′-oxydiphenyl)-phosphinic acid by polycoordination in the melt at 175−200°C. In contrast to homopolymers, the mixed chromium polyphosphinates based on the above acid are fully soluble in chloroform and have molecular weights up to 10 000.

V. SYNTHESIS OF OTHER COORDINATION POLYMERS WITH INORGANIC MAIN CHAINS

Comparatively few studies dealing with coordination polymers containing bridge ligands other than phosphinate anions have been published. The synthesis of coordination bridge polymers based on phosphinomonothioic and phosphinodithioic acids containing cobalt, manganese, uranyl, and chromium in the inorganic main chain has been described [43,63,104,109-112]. For example, the interaction of diethyl- and diphenyl-phosphinothioic and diethyl- and diphenyl-phosphinodithioic acids with cobalt and uranyl acetates in benzene or ethanol yielded polyphosphinomonothioates and polyphosphinodithioates with molecular weights of 3000−6000. [63]

Callicaris et al. [112] showed that, in contrast to zinc polydiethylphosphinate, zinc diethylphosphinodithioate has a dimeric structure, which led the authors to the conclusion that phosphinodithioic acids are much less capable of forming polymers with metal ions than their phosphinomonothioic and phosphinic analogues.

Owens et al. [113] described a tin-containing polymer based on methylphosphonic acid, which was obtained by the pyrolysis of a tin tetrachloride complex of di-isopropyl methylphosphonate at 140−190°C and had the following structure:



Korshak and coworkers [68,114] achieved the oxidative decarbonylation of the metal carbonyls $M_2(CO)_{10}$, $Fe(CO)_5$, $Fe_2(CO)_9$, $W(CO)_6$, and $Cr(CO)_6$ by toluene-*p*-sulphonic acid. Toluene-*p*-sulphonic acid was also used as the ligand in polycoordination with manganese acetate. The molecular weight of the polymer from manganese acetate and toluene-*p*-sulphonic acid, determined by the light scattering method, proved to be 16 200 and that of the polymer from iron pentacarbonyl and toluene-*p*-sulphonic acid was 7900.

Korshak and coworkers [67,68,115] obtained metal polyarsinates by the reaction of diphenylarsinic acid with iron, chromium, manganese, and tungsten carbonyls and also with manganese and zinc acetates. The tungsten polyarsinate contained residual carbonyl groups and the degree of its polymerisation was 3-4. [115]

Metal polyarsinates, some of which proved soluble in water, were synthesised by the polycoordination of di-n-alkylarsinic acids with zinc acetate and chromium nitrate in solution [86,116].

VI. PROPERTIES OF COORDINATION POLYMERS WITH INORGANIC MAIN CHAINS

Metal polyphosphinates are usually powdered substances. Some of them have a characteristic colour (for example cobalt polyphosphinates are pale-blue and chromium polyphosphinates are green). The Table shows that certain metal phosphinates exhibit a high thermal stability. For example beryllium polydimethyl- and polydibutylphosphinates have melting points of 465° and 452°C respectively [51]. Polyphosphinates based on acids with aromatic substituents at the phosphorus atom are as a rule infusible, but cobalt polymethylphenylphosphinate and also certain mixed polyphosphinates whose chain contains the anions of both aromatic and aliphatic phosphinic acids are capable of passing to a fluid state [23,24,51].

X-Ray diffraction studies on metal phosphinates showed that they usually have a crystalline structure [11,22,24-33,35-44,58].

Crystalline polyphosphinates can be converted into an amorphous form by rapid cooling of the polymer melts. A characteristic feature of bivalent metal (zinc and cobalt) polydialkylphosphinates in the amorphous form is their high frost resistance. For example, amorphous zinc polydi-n-butylphosphinate with a molecular weight of about 10000, obtained by rapid cooling of the polymer melt (150°C), had a brittleness temperature of −40°C.[22] Mixed bivalent metal polyphosphinates have even lower brittleness temperatures. Thus zinc polyphosphinate based on di-n-butyl- and di-n-octyl-phosphinic acids remained elastic down to −100°C.[22,54]

Amorphous metal homopolyphosphinates crystallise slowly at room temperature, but certain mixed coordination polymers in the amorphous form do not show a tendency towards crystallisation at the usual temperatures[22].

Giancotti, Giordano, and coworkers[38] explained the high elasticity of mixed polymers by the disordered distribution of their alkyl side groups at the phosphorus atom on the basis of X-ray diffraction and differential thermographic studies.

Giancotti et al.[42] observed solid-phase transitions between two crystalline forms of zinc polyphosphinates between −13° and 77°C. They showed that above the transition temperature, i.e. in the β-form, the carbon chains of the aliphatic substituents at the phosphorus atom are flexible and capable of twisting; they are more ordered in the α-form.

Bivalent metal polyphosphinates with aliphatic substituents at the phosphorus atom are completely or partly soluble in organic solvents[22,24,38,51,57,69]. Homopolyphosphinates with aromatic substituents are largely insoluble[23,51,65].

Korshak, Krukovskii, and coworkers showed[56] that the solubility of mixed zinc polyphosphinates based on di-n-butylphosphinic acid, which also contain the residues of diphenyl-, distyryl-, and 2,2′-(4,4′-dimethyl-1,1′-oxydiphenyl)-phosphinic acids, increases with increase of the content of dibutylphosphinate groups in the polymer.

Mixed bivalent metal polyphosphinates based on phosphinic acids containing only aliphatic alkyl substituents at the phosphorus atom showed the highest solubility[22,38].

The available literature data on the behaviour of metal polyphosphinates in solution are difficult to compare, since they refer to polyphosphinates containing in the chain metal atoms of different valence. Furthermore, different experimental techniques were used in the investigations.

Thus the viscosity of solutions of chromium polydiphosphinate $\{Cr(H_2O)(OH)[OP(C_6H_5)_2O]_2\}_n$ in chloroform was found to increase with time; after keeping the polymer in chloroform at 55°C for several days, the intrinsic viscosity increased from 0.03−0.04 to 1.0 dl g^{-1}.[32,34]

Slota et al. observed a decrease of the molecular weights of beryllium-containing polyphosphinates with time in different solvents[53,55].

Examination of the relations quoted in a number of studies between the intrinsic viscosities of metal polyphosphinate solutions and polymer concentration shows that they are not linear. The intrinsic viscosities of solutions of many polymers increase sharply with increase of the concentration[22,23,44,56], which has been attributed[56] to the instability of metal polyphosphinates in solution.

The explanation of such concentration variation of the intrinsic viscosities of metal polyphosphinates by the aggregation of the molecules of the coordination polymer as a result of hydrogen bonding[55] is apparently invalid in the light of the results of Kuchen and Hertel[110], who showed that the concentration variation (in benzene) of the molecular weight of cobalt polydiethylphosphinothioate is the same at 37°, 45°, and 60°C. This suggests that the bond strengths in the association complexes are much higher than those of hydrogen bonds.

Korshak et al. showed[57] that 0.5−1% solutions of metal polyphosphinates in benzene and toluene are stable over a period of time. However, measurements of the intrinsic viscosities of manganese and zinc polyphosphinate solutions in benzene and toluene at different concentrations revealed a sharp decrease of the intrinsic viscosity with dilution of the solution. The anomalously low intrinsic viscosities of dilute manganese and zinc polyphosphinate solutions indicate the degradation of the macromolecules in solutions at low concentrations.

Indeed measurements of the molecular weight of manganese polydi-n-octylphosphinate in benzene by the ebullioscopic method and of zinc polydi-n-heptylphosphinate in the same solvent by sedimentation in an ultracentrifuge showed that the molecular weights of these polymers decrease sharply in both cases with decrease of the concentration of the solutions.

It has been shown for metal polydialkylphosphinates that the degradation of bivalent metal polyphosphinates in organic solvents is reversible and takes place almost instantaneously when the solution is diluted even at room temperature.

Delman et al.[117] demonstrated the high polydispersity of chromium polyphosphinates determined by the gel-chromatographic method.

In certain studies attempts were made to prepare films from coordination polymers[22,51,54,64,80,82,87]. However, non-plasticised films prepared from melts or solutions of homopolyphosphinates are brittle[82]. Their elasticity can be improved by the introduction of 20−60% of a plasticiser relative to the weight of the polymer. Thus a film containing 30% of the "Aroclor 1254" plasticiser and having a tensile strength of 133 kgf cm^{-2} was obtained from a polymer based on bivalent chromium acetate and diphenylphosphinic acid (molecular weight about 10000).[30]

American investigators[82,86,87] described the preparation of moulded articles, transparent films, and fibres from a chromium-containing polytriphosphinate obtained by the cross-linking of linear polymers of the type $\{Cr(H_2O)(OH)[OPRR'O]_2\}_n$ with low-molecular-weight cross-linking agents, which consisted of acid having the general formula R′R″P(O)OH.

Mixed polymer films are very elastic. A thin film, which did not change its size up to 100°C and remained flexible on cooling down to −100°C, was obtained from a mixed zinc polymer based on di-n-butyl- and di-n-octylphosphinic acids (molecular weight 10000) by pressing at about 150°C.[22,54]

The thermal stabilities of coordination polymers with inorganic main chains were estimated from thermogravimetric data. It was found that they depend both on the nature of the metal entering into the coordination centre and on the structure of the ligand forming the bridge group. Thus various metal polydiphenylphosphinates can be arranged in the following series in terms of the temperatures corresponding to 10% increase of their weight in an inert atmosphere (at a heating rate of 5 deg min^{-1}):

$$Mn(580°) < (Zn(520°) > W(510°) > Fe(453°) > Mo(425°) > Cr(390°)[67,102].$$

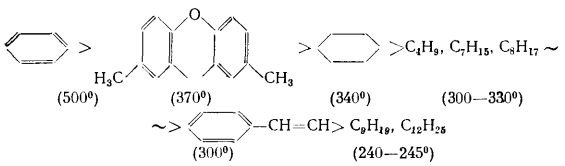
When the given ligand is replaced by a diphenylarsinic acid residue, the thermal stability of the corresponding coordination polymers falls and the relative stability series of the metals changes:

$$Cr\,(390^0) > Fe\,(380^0) > Mo\,(360^0) > W\,(320^0) > Mn\,(240^0)\ ^{67}.$$

Polymers based on toluene-*p*-sulphonic acid exhibit the highest thermal stability. Thus manganese polysulphonate does not begin to decompose in an inert atmosphere until 520°C and its weight decrease by 10% at 600°C.[67,114]

According to thermogravimetric data (heating rate 4.5 deg min^{-1}), the weight of coordination polymers based on phosphinic acids with aliphatic substituents at the phosphorus atom begins to decrease in air at a temperature as low as 160–230°C.[57,69,102]

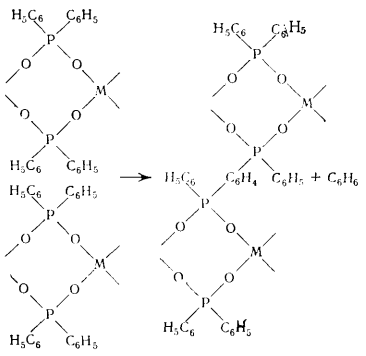
It has been established that manganese polyphosphinates form the following sequence of substituents at the phosphorus atom as a function of the temperature (indicated in brackets) corresponding to the 10% decrease in the weight of the polymer in air at a heating rate of 4.5 deg min^{-1}:



Among the bivalent metal polyphosphinates described, cobalt polydiphenylphosphinate proved to have the highest thermal stability: its weight begins to decrease in an inert atmosphere at 485°C.[24]

Investigations have shown[23,24,51,63] that the alkyl or aryl groups at the phosphorus atom are the first to be split off in the thermal degradation of bivalent metal polyphosphinates.

Only benzene has been detected in the volatile decomposition products of zinc polydiphenylphosphinate at 500°C; it is probably liberated via the mechanism[24]



Golgotui and Rosca[63] noted that the most stable bonds in metal polyphosphinates are the O–M and O–P linkages in the inorganic main chain of the macromolecules, which persist in the solid decomposition products characterised as $M(PO_3)_2$ or $MO.P_2O_5$. According to Saraceno and Block[32], chromium polyphosphinates with the structure $\{Cr(H_2O)(OH)[OP(C_6H_5)_2O]_2\}_n$ begin to lose weight at about 375°C in dry nitrogen, at 355°C in air, and at 335°C in moist oxygen. The authors attribute the initial decrease of the weight of the polymers at 370–420°C to the elimination of the residual acetate groups from the polymer and not to its true decomposition.

Comparison of the temperatures corresponding to the onset of weight loss by chromium polydiphosphinate (296 to 300°C), obtained from chromium acetylacetonate and diphenylphosphinic acid, and chromium acetylacetonate itself (approximately 250°C)[118] led Block et al.[15] to the conclusion that the side ligand at the chromium atom (acetylacetone) is the first to be split off on heat treatment.

The study of beryllium[51], chromium[32], zinc[23], and manganese[102] polyphosphinates subjected to a prolonged heat treatment under isothermal conditions revealed a fairly high thermal stability. Thus, on heating in air at 440°C for 20 h, zinc polydiphenylphosphinate lost only about 2.8% of its weight[23].

The literature data available at present therefore permit the conclusion that the thermal decomposition of metal polyphosphinates does not involve the inorganic main chain in the initial stage and proceeds as a result of the elimination of the organic substituents at the phosphorus atom or the additional ligands linked to the metal atom.

When the oxygen atom is replaced by sulphur in the phosphinate group, the thermal stability of the polymers diminishes. This can be traced on the basis of the results of the thermogravimetric analysis of cobalt-containing coordination polymers based on diethylphosphinic, diethylphosphinothioic, and diethylphosphinodithioic acids[63]. These polymers can be arranged in the following series in terms of the temperatures corresponding to the onset of their weight loss in air:

$$\underset{(285^0)}{\{Co[(C_2H_5)_2PO_2]_2\}_n} > \underset{(195^0)}{\{Co[(C_2H_5)_2POS]_2\}_n} > \underset{(185^0)}{\{Co[(C_2H_5)_2PS_2]_2\}_n}$$

The chemical stability of metal polyphosphinates has been very little studied. It has been shown that pyridine has a degrading effect on zinc polydi-n-butylphosphinate[56] The dissolution of cobalt polydiphenylphosphinate in pyridine is accompanied by the formation of adducts in which the phosphinate : pyridine ratio is 1 : 1.[18]

Slota et al.[53] studied the degrading influence of water on beryllium-containing polyphosphinates and suggested that the bonds formed by the residues of the phosphonic acid, present as an admixture in the initial phosphinic acid, are unstable with respect to hydrolysis.

Under the influence of concentrated inorganic acids and bases, bivalent metal polyphosphinates decompose with the liberation of the corresponding phosphinic acids even at room temperature. Acetic acid degrades polymers to a much smaller extent. Manganese polyphosphinates with aliphatic substituents and zinc polyphosphinate resist the action of water[102].

Rose and Block[23] noted the stability of zinc polyphosphinates with respect to radiation.

The resistance of metal polyphosphinates to the action of water together with their high thermal stability and heat resistance constitutes an important factor, which provides a basis for the development of various materials from them. However, there is so far very little information about the practical applications of bridge coordination polymers. It is contained mainly in the patent literature. In particular, it has been noted that polyphosphinates can be used as protective coatings[119]. Titanium and chromium polyphosphinates as components of coatings impart antistatic properties to organic plastics[120]. The study of the influence of metal polyphosphinates on the polymerisation of aminoalkyl acrylates showed that metal polyphosphinates are responsible for the formation of gel-like structures in the monomer at low concentrations (of the order of several per cent). It has been shown that the

introduction of small amounts of polyphosphinates into the initial monomeric composition gives rise to a structural viscosity, which is reflected in the supermolecular structure and improves the physicomechanical properties of the coatings based on the polymers [59,121].

Certain chromium triphosphinate polymers can be used as thickening agents for silicones which enables them to be used at elevated pressures [120,122].

According to an American patent [123], chromium polyphosphinate additives are used as photostabilisers and thermostabilisers for poly(vinyl chloride) and its copolymers. Chromium polymethylphenylphosphinate is a satisfactory stabiliser of the viscosity of greases and hydraulic liquids based on phosphate esters (for example, tricresyl phosphate) [124]. Heat resistant (up to 300°C) metal polyphosphinates manufactured in the USA are recommended as coatings, composition for the formation of hermetic seals, and adhesives [125].

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Dissociation of Positive Molecular Ions

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The dissociation of accelerated positive molecular ions on collision with atoms and molecules (impact dissociation) is considered. Various experimental methods for the investigation of such dissociation are compared. The mechanisms of the impact dissociation of molecular ions are examined in relation to the simplest diatomic ions. Attention is concentrated on the impact dissociation of polyatomic ions. The scope of this in the determination of the structures and energetics of excited ions is discussed.
The bibliography includes 120 references.

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I. INTRODUCTION

The study of the structures and excitation energies of ions yields much information about the structure and state of the initial neutral molecule; furthermore, it has additional interest, since ions arise and are involved in various processes and information about their structures and excitation energies can be used to characterise such processes.

The structures and excitation energies of ions can be studied by mass-spectroscopy using different procedures, in particular it is possible to investigate their spontaneous dissociation or their dissociation under the influence of various agents, i.e. induced or impact dissociation. The spontaneous dissociation of molecular ions is already used in mass-spectrometry to determine the mechanisms of the dissociation of the initial ion, to determine the structure of the ion, to classify the transition states leading to a specific reaction, and to obtain analytical information about mixtures. Impact dissociation reactions of molecular ions can yield more information about the ion and the initial molecule than spontaneous dissociation, particularly because they can occur with any ion and via numerous channels. The impact dissociation of ions can be achieved by the same procedures as the ionisation of molecules, i.e. as a result of the collision of electrons and protons, but with ions and not molecules. This excites the initial ions (they can actually be ionised further) and causes their dissociation, yielding their fragmentation spectra, which can be called the mass spectra of the ions by analogy with the mass spectra of molecules. The mass spectra of both positive and negative ions can be studied in this way. However, the study of the dissociation of ions under the influence of electrons and photons is only just beginning and so far only the first experiments have been carried out with the simplest ions.

This is due to considerable technical difficulties in studies of this kind, although there is no doubt that this procedure will yield more accurate answers to many questions concerning the structures and the energy states of ions and the mechanisms of their dissociation of accelerated ions by collisions with atoms and molecules.

In experiments designed to investigate impact dissociation one measures the total dissociation cross-sections, the relative probabilities of the formation of various fragments (dissociation spectra), and the angular and energy distributions of the dissociation products. Many characteristics of impact dissociation have been observed and investigated; these yield conclusions concerning the structures and excitation energies of the initial ions and also concerning the mechanisms of their decomposition.

The present review is devoted mainly to studies on the dissociation of polyatomic ions and its aim is not to cover the majority of investigations in this field. The fundamental characteristics of impact dissociation were discovered by the present authors on the basis of experiments carried out mainly at the Karpov Physicochemical Institute. The dissociation of diatomic molecular ions is considered only in order to examine the mechanisms of impact dissociation. The entire vast experimental and theoretical data on the dissociation of the simplest molecular ions evidently merit separate consideration.

II. EXPERIMENTAL METHODS FOR THE INVESTIGATION OF THE DISSOCIATION OF IONS

There are several groups of investigators of the dissociation of ions, who are using the usual analytical mass-spectrometers without any significant modification, i.e. in approximately the same way as in the work of Aston[1], who first observed the dissociation of H_2^+ ions on collision with the molecules of the residual gases. However, it is already clear that, by employing the usual mass-spectrometers with a single analyser, it is possible to obtain only very limited information about the dissociation processes of molecular ions. For this reason, in order to study in detail the ion dissociation reactions and hence obtain information about their mechanisms and about the structures and excitation energies of the ions and of the initial molecules, it is necessary to apply a modified mass-spectrometric technique, which involves at least two analysers and a collision chamber.

In a sector mass-spectrometer with a single magnetic analyser dissociation is usually observed in the region where there is no magnetic field between the outlet slit of the ion source and the magnet and it can occur both as a result of collisions with the molecules of residual gases and spontaneously. The fragment ions then give diffuse peaks in the collector, the so called Aston bands or "fractional" peaks, the positions of which on the mass scale are defined by the formula

$$m^* = \frac{m_f^2 q_i}{m_i q_f^2}, \qquad (1)$$

where m^* is the apparent mass of the fragment ion, m_f and q_f are the true mass and charge of the fragment ion, and m_i and q_i are the mass and charge of the initial ion. This formula was obtained on the assumption that the velocity of the ion does not change significantly on decomposition. This is in fact found to be the case in the experiments. If the charge does not change either in the decomposition of the initial singly-charged ion, Eqn. (1) simplifies to

$$m^* = \frac{m_f^2}{m_i}. \qquad (2)$$

On the other hand, if the ion decomposes in the ion source during the acceleration process, the apparent mass of the fragment ion is defined by the formula[2]

$$m^* = \left(\frac{m_f^2 q_i}{m_i q_f^2} \cdot \frac{V_1}{V}\right) + \left(1 - \frac{V_1}{V}\right)\frac{m_f}{q_f}, \qquad (3)$$

where V_1 is the potential difference corresponding to the distance traversed by the metastable ion before the decomposition point and V is the total accelerating potential difference.

The use of a mass-spectrometer with a single magnetic analyser to investigate ion dissociation suffers from the disadvantages that, in the region between the ion source and the magnetic analyser, all the ions emerging from the ion source can dissociate. As a result, the peaks corresponding to different dissociation processes can be superimposed. In particular, this hinders the observation of spontaneous and impact dissociation in the ionisation of polyatomic molecules. The absence of a localised gas target (collision chamber) hinders the determination of the collision cross-sections. The technique for the investigation of the dissociation of the simplest ions in a usual mass-spectrometer has been described[3].

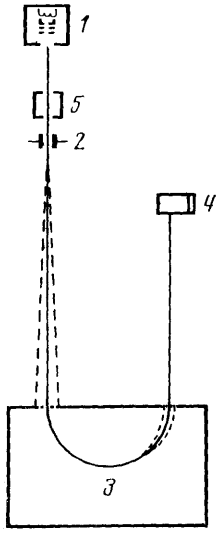

Figure 1. Schematic illustration of a mass-spectrometer: 1) ion source; 2) electrostatic deflector; 3) magnetic analyser; 4) ion detector; 5) collision chamber.

Thus mass-spectrometers with a single magnetic analyser are at present used mainly to investigate the dissociation of the simplest diatomic and triatomic molecular ions. Modified designs of such apparatus have been used by Los[4] and Durup et al.[5] Fig. 1 presents a schematic illustration of Los's apparatus. In contrast to the usual mass-spectrometers, it incorporates a collision

chamber *5*. The presence of narrow collimators at the outlet from the collision chamber makes it possible to achieve a high angular resolution (10^{-3} rad). The analysing magnet has an inhomogeneous field, which results in a high resolving power with respect to energy ($\sim 10^{-4}$).

The disadvantages of single mass-spectrometers are eliminated in apparatus with two magnetic analysers (double mass-spectrometers), which were used for the first time to investigate the impact dissociation of the simplest diatomic and triatomic ions by Ioffe[6-9] at the Leningrad Physicotechnical Institute.

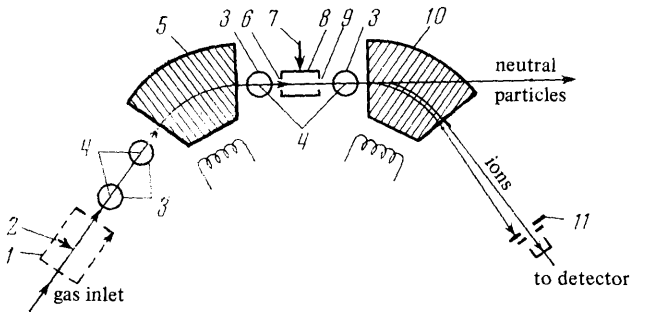

Figure 2. Schematic illustration of a double mass-spectrometer: 1) ion source; 2) electron beam; 3) diffusion pumps; 4) electronic valves of the ionisation manometer; 5) mass-monochromator; 6) inlet slit S_1 of the collision chamber; 7) admission of target gas; 8) collision chamber; 9) outlet slit S_2 of the collision chamber; 10) mass analyser; 11) the slit S_3 before the ion collector.

Studies on the dissociation of polyatomic ions using double mass-spectrometers have begun at the Karpov Physicochemical Institute[10-12]; a schematic diagram of one of these instruments is presented in Fig. 2. The first magnetic analyser (mass-monochromator) isolates the beam of the ions being investigated and directs them to the collision chamber which has controllable inlet and outlet slits S_1 and S_2. Beyond the chamber, there is a second magnetic analyser (the mass-analyser) which analyses the spectrum of the fragments arising as a result of impact or spontaneous dissociation. The width of the slit S_3 before the collector varies in the range 0–16 mm. The differential evacuation of the mass-spectrometer is achieved by four diffusion pumps, which give a pumping rate of 100 litre s^{-1}. The ion source consists of a gas source with ionisation of the molecules by an electron beam with a controllable energy. The accelerating potential varies from 2 to 5 kV. Furthermore, there is a possibility of a further acceleration of the ions up to 100 keV. On a double mass-spectrometer, it is possible to investigate both the spontaneous dissociation of the metastable ions and the dissociation resulting from single collisions of the accelerated ions with the molecules of the gas admitted to the collision chamber up to a pressure of 10^{-4} torr, measured with the aid of a calibrated ionisation manometer or a McLeod gauge.

The total dissociation cross-section of the ions σ is calculated from the formula

$$\sigma = \frac{I^* kT}{Ipl}, \qquad (4)$$

where I^* is the current due to the secondary fragment ions, I the current due to the initial ions, p the gas pressure in the collision chamber, l the effective length of the collision chamber†, k the Boltzmann constant, and T the absolute temperature of the gas in the chamber.

For single collisions I^*/I varies linearly with pressure and the dissociation cross-section is characterised by the slope of the linear plot of I^*/I against p. Fig. 3 illustrates relations of this kind for a number of dissociation processes of ions derived from ethylene. Extrapolation of the I^*/I–p straight lines to zero pressure yields intercepts on the ordinate axis, which characterise the contribution of spontaneous decompositions to the given dissociation process.

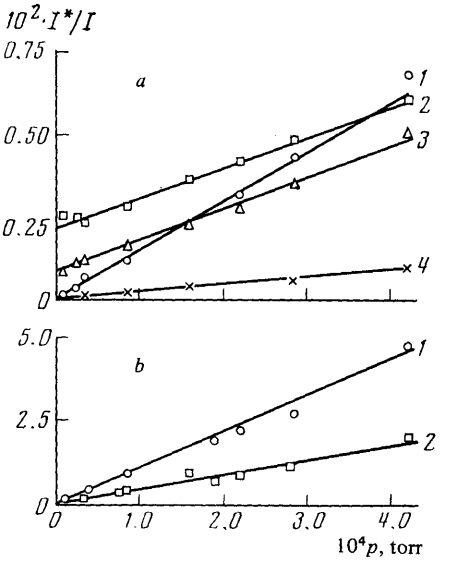

Figure 3. Variation of the relative ionic currents (I^*/I) with gas pressure p (measured using an LM-2 gauge) in the collision chamber. *a*: 1) $C_2H_4^{2+} \rightarrow C_2H_4^+$; 2) $C_2H_4^{2+} \rightarrow C_2H_3^+ + H^+$; 3) $C_2H_4^{2+} \rightarrow C_2H_2^+ + H_2^+$; 4) $C_2H_4^{2+} \rightarrow C_2H^+$; *b*: 1) $CH_2^+ \rightarrow CH^+ + H$; 2) $CH_2^+ \rightarrow C^+$.

To determine the true extent of spontaneous decomposition, it is always necessary to investigate the relation between the ratio I^*/I and the pressure in the region where it occurs, as has been done in studies on a double mass-spectrometer. In certain other investigations the pressure was not measured directly in the region where ions are decomposed but measurements were made of parameters such as the pressure in the system for supplying the ion source with gas[16] or of the current due to the initial ions[17], which is proportional to the gas pressure in the ion source. A situation may arise where the pressure in the region where ions decompose varies only slightly

† It is as a rule greater than the geometrical length of the collision chamber. The methods for its calculation have been described[13,14] and in the study of Menendes et al.[15] the collision region was isolated by an electric field.

when the pressure in the filling system is altered (for example with a high pumping rate in this region and when it is remote from the source) and is close to the background (residual) pressure. Then, when dissociation occurs on collision with the molecules of the background gas, the ratio I^*/I will vary only slightly as a function of the pressure measured in this way, creating the impression that it is apparently independent of pressure. One cannot rule out the possibility that such a situation arose under the conditions used by Wankenne and Momigny[17]. Extrapolation of this relation to zero pressure (in the measurement of p by the above methods) leads to an incorrect determination of the contribution by the spontaneous decomposition of the metastable ions. For this reason, the pressure must be measured directly in the region where decomposition is observed.

For a more complete understanding of the impact dissociation process, it is necessary to carry out investigations for different kinetic energies of the initial ions, particularly in the region of threshold energies, which permits the determination of the dissociation and excitation energies of the ions. A number of instruments have been constructed[18-20] for the investigation of dissociation under the conditions of low energies.

Double-focussing mass-spectrometers have been used recently to study ion dissociation. In such instruments there are three regions in which it is possible to observe the dissociation of metastable ions[21]. The first region is between the inlet slit of the ion source and the inlet to the electrostatic analyser. The second region is between the electrostatic and magnetic analysers and the third region is located in the accelerating section of the ion source. In the study of spontaneous decompositions in the first region the defocussing method is used. The double-focussing mass-spectrometer transmits only ions with a narrow range of kinetic energies. Ions formed on spontaneous decomposition possess only part of the energy of the initial ion. To detect the metastable ion in the reaction $m_0^+ \rightarrow m_1^+$, it is necessary to increase the ratio of the accelerating potential V to the potential on the plates of the electrostatic analyser E by the factor m_0/m_1, i.e. the mass-spectrometer must be defocussed in relation to the initial ion[22]. This can be done by scanning the accelerating potential from its usual value corresponding to a constant potential E using a magnetic field tuned for the transmission of the ion with the mass m_1. The spectrum of all the ions generated on spontaneous decomposition by the ions with the mass m_1 can be obtained in this way.

In another method[23-25] the peaks corresponding to the decomposition of the metastable ions are observed by decreasing the potential applied to the electrostatic analyser by the factor m_1/m_0 and by tuning the magnetic field for the transmission of the "apparent mass" $m^* = m_1^2/m_0$. The advantage of this method over the first procedure is that, in carrying out quantitative measurements, the intensities of different metastable transitions can be more effectively compared under the same conditions in the ion source, in particular at a constant accelerating potential.

The technique for the investigation of spontaneous dissociation in a double-focussing mass-spectrometer having the Nier–Jones geometry, with scanning of the potential applied to the electrostatic condenser, has been described in relation to the decomposition of the ions formed from the toluene molecule[26]. The sensitivity achieved in recording the ions generated on decomposition amounted to $(1 - 2) \times 10^{-6}$ of the intensity of the initial ion, i.e. about 10^{-4}%.

McLafferty and coworkers[27] used a mass-spectrometer with the reverse geometry. Here the ion source in the double-focussing instrument was located in the place of the detector and the detector was in the place of the ion source. Spontaneous decompositions are recorded in the region between the magnetic and electrostatic analysers. This method has certain advantages compared with the other two procedures described above. The scanning of the potential applied to the electrostatic condenser yields the entire spectrum of the fragment ions obtained from the given initial ion. Ion dissociation on collision is now also beginning to be investigated on apparatus with double-focussing having both normal and reverse geometry[28].

In the study of ion dissociation the measurement of the angular and energy distributions of the dissociation products is important. To measure the angular distributions of ions in double mass-spectrometers, it must be possible to move the second analyser relative to the axis passing through the centre of the collision chamber, as for example in the apparatus illustrated in Fig. 2. Another method has been used in studies[4,5] where a deflecting collimator was mounted at the outlet from the collision chamber and was able to scan the ion beam via a narrow collimator.

The energy distribution is measured with the aid of magnetic[4,5] or electrostatic analysers. A method for the energy spectroscopy of ions using a double-focussing mass-spectrometer, which makes it possible to record the changes in the energy of the fragment, equal to 10^{-4} eV in the centre of mass system for a dissociating ion, has been reported[29]. A novel apparatus using a 127° electrostatic analyser and a quadrupole mass-analyser, which were positioned beyond the collision chamber, has been used to measure the angular and energy distributions of the dissociation products of certain diatomic ions[30]. The nature of the energy distribution of the dissociation products is important, since the efficiency of the recording of the fragment ions depends on it. When it is necessary to measure the total dissociation cross-section, all the fragment ions formed in the collision chamber should be recorded in the collector. This is most important also for the comparison of the intensities of different metastable transitions. Incomplete recording of the protons has been the cause of an error in the measurement of the total dissociation cross-section of the H_2^+ ions in certain early investigations, discussed in a number of communications[13,14,31].

In the measurement of the total dissociation cross-sections of simple diatomic and triatomic ions, where there is no need for a high resolution, the slit before the ion collector must be as wide as possible. Sometimes it must also be made wide in the study of the dissociation of polyatomic ions[32]. This is difficult to achieve in analytical mass-spectrometers. For a narrow slit, it is necessary to measure the distribution of the peak intensity by scanning the magnetic field and the total current must be found by integrating this distribution. In double-focussing apparatus this procedure is more complicated, since it is necessary to scan the electric and magnetic fields[33]. Quantitative analysis of metastable transitions involving polyatomic ions may be experimentally difficult, requiring the use of a computer, as was done by Coutant and McLafferty[34].

In concluding this section, we shall consider briefly a method for the investigation of ion dissociation under the influence of electron and photon impact. The dissociation in collisions with electrons is studied by the method of ion and electron beams intersecting at right angles. To

reduce the signal arising due to the impact dissociation of the initial ions in collisions with the molecules of the background gas, the pressure in the region of the intersection of the beams is less than 10^{-9} torr. Furthermore, a technique involving modulation of the peaks is employed to isolate the required signal. Measurements have been made of the dissociation cross-sections of H_2^+, O_2^+, N_2^+, and D_2^+ for electron energies in the range 10–1500 eV.[35]

Using the emission from a ruby laser to investigate the photodissociation of H_2^+ ions[36], the energy spectrum of the protons was found to depend on the plane of the polarisation of the light and vibrational structure was observed, reflecting the populations of the vibrational levels of the initial H_2^+ ions. Thus the study of the photodissociation of molecular ions by means of laser light with simultaneous analysis of the dissociation products with respect to kinetic energies may prove to be promising in the sense of creating a desirable method for determining the excitation energies of molecular ions obtained in different processes. Still greater possibilities arise when tunable lasers are used.

III. DISSOCIATIVE COLLISIONS OF DIATOMIC IONS

The studies on the impact dissociation of diatomic ions carried out up to 1970 have been reviewed in a book[37] and two articles[38,39]. The aim of this section is to describe the fundamental mechanisms of the impact dissociation of accelerated ions with illustrations by examples taken mainly from the recent studies in this field.

The impact dissociation of a diatomic ion proceeds via the mechanism

$$AB^+ + M \begin{cases} \longrightarrow A^+ + B + M \\ \longrightarrow B^+ + A + M \end{cases}, \qquad (5)$$

where all the species on the right-hand side can also be formed in excited states and, for high kinetic energies, in ionised states.

The dissociation mechanisms have been classified by Durup[38], the classification having been somewhat modified by Los[4]. Four mechanisms can be put forward for the impact dissociation of molecular ions: (1) electronic transitions to unbound states of the molecular ion or to bound states above the dissociation limit; (2) vibrational-rotational transitions to a continuum without a change in the electronic state of the ion AB^+ (adiabatic mechanism); (3) dissociation via the formation of an intermediate complex (AB^+M), which decompose into $A^+ + B + M$ or into $B^+ + A + M$, which occurs when the energies of the relative motion are of the order of magnitude of the bond energy of the AB^+ ion; (4) predissociation caused by the collision.

The contribution of each mechanism to the total dissociation cross-section depends to a large extent on the kinetic energy E_0 of the AB^+ ion and also on its excitation. Since ion dissociation has been studied over an extremely wide range of values of E_0 (from several electron-volts to tens of MeV for H_2^+ ions), it is possible to estimate the approximate limits of the region of E_0 within which a particular mechanism predominates. Electronic transitions predominate over a wide range of energies from hundreds of electron-volts to the maximum values achieved experimentally. Vibrational transitions are probably important for energies in the range 10–100 eV. Finally, induced predissociation has been observed for energies in the range $\sim 10^3$–10^4 eV.

There is an unambiguous relation between the distribution of the dissociation products in the centre of mass coordinates based on the AB^+ ion and the form of the distribution in terms of the laboratory coordinate system, or, using the mass-spectrometric terminology, the shape of the peak in the ion collector. We may note that, in order to obtain the true energy distribution in the centre of mass coordinates on transformation from the distribution in terms of the laboratory coordinate system, account must be taken of the apparatus function of the instrument[5,40]. The relation between the shape of the peak and the energy distribution of the dissociation products for double-focussing mass-spectrometers has been considered[41,42]. There is a simple relation between the energy in the centre of mass system and the energy E_A of the fragment ion in terms of the laboratory system. For convenience we shall assume that the masses of the species A and B involved in reaction (5) are $m_A = m_B = m$. If the velocity of the fragment in the centre of mass system is u, then

$$E_A = \frac{m(v_0 + u)^2}{2} = \frac{mv_0^2}{2} + mv_0 u\cos\varphi + \frac{mu^2}{2} = \frac{E_0}{2} + \frac{W}{2} + mv_0 u\cos\varphi, \qquad (6)$$

where v_0 is the velocity of the AB^+ ion, φ the angle at which the A^+ ion is ejected in the (A, B) centre of mass system, W the kinetic energy of the dissociation products in the (A, B) centre of mass system, and E_0 the kinetic energy of the initial AB^+ ion. The quantity $\frac{1}{2}W + mv_0 u\cos\varphi = \Delta E$ is the additional kinetic energy acquired by the A^+ ion in the laboratory system of coordinates.

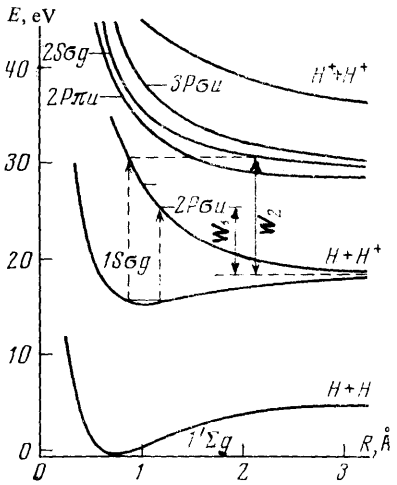

Figure 4. Potential energy curves for H_2^+ ions.

We shall consider this in relation to the dissociation of H_2^+ ions, the potential energy curves for which are shown in Fig. 4. In the electronic transition from a particular vibrational level in the ground state $1s\sigma_g$ to the nearest unbound state $2p\sigma_u$ in the centre of mass system a kinetic energy in the range from W_1 to W_2 is liberated, since for $E_0 \simeq 10^3$ eV and above the collision time is much shorter than the vibration period of the nuclei and the Franck–Condon principle is maintained in the electronic transition.

The limits W_1 and W_2 are determined by the initial vibrational level of the H_2^+ ion. In the measurement of the energy distributions use is made of narrow outlet collimators, which isolate the fragment ions emerging in the centre of mass system at angles close to $\varphi = 0°$ and 180°. Then, in accordance with Eqn. (6), two energies are observed in terms of the laboratory system for each energy of the fragment in the $\frac{1}{2}W$ centre of mass system (and the corresponding velocity u):

$$E_1 = \frac{E_0}{2} + mv_0u + \frac{1}{2}W;$$

$$E_1' = \frac{E_0}{2} - mv_0u + \frac{1}{2}W.$$

Thus in the laboratory coordinate system an energy distribution with two symmetrical maxima will be observed. The maxima will be diffuse owing to the contributions of different W acquired by the dissociation products of the AB^+ ions in a particular initial vibrational state and in consequence of a distribution with respect to vibrational states in the beam of the initial H_2^+ ions. Since in reality the outlet slits of the instruments have a finite width and transmit a proportion of the ions with a transverse velocity component u, the form of the distribution changes, since the number of ions detected increases for $\Delta E \simeq 0$ [the values of W in Eqn. (6) can be neglected, since $W \ll E_0$].

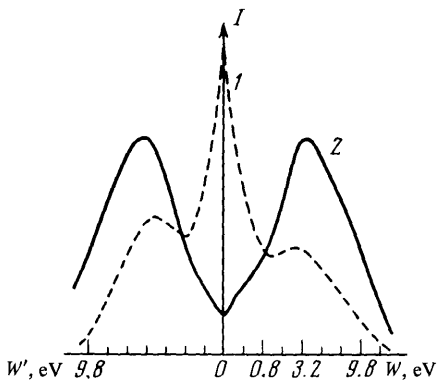

Figure 5. The energy spectrum of H^+ ions in the centre of mass system on impact dissociation of H_2^+: 1) without allowance for the apparatus function; 2) with allowance for the apparatus function.

Therefore a sharp peak appears at the centre of the distribution (Fig. 5). Transitions for which $W \simeq 0$ make a definite contribution to this maximum; these are vibrational transitions to the continuum of the $1s\sigma_g$ state adjoining the dissociation limit. The contribution of the vibrational transitions increases with increase of the atomic number of the target[38,40]. Some workers believe that electronic transitions to the $2p\sigma_u$ state from high vibrational levels of the ground state make a significant contribution to the formation of the central peak[43]. The possibility of dissociation via the excited state $2p\pi_u$, which has a low-slope potential curve, is also assumed. A shift of the central peak towards lower energies has been observed in experiments with different targets, particularly when the excitation energy of the target is small[38,44]. The position of the central peak is determined by the quantity $E_0/2 - E^*/2$, where E^* is the energy consumed in the dissociation process (the excitation energy of the particles involved in the collision).

The angular distributions of the protons in the dissociation of accelerated H_2^+ ions have been studied both theoretically and experimentally. A calculation carried out for different internuclear distances R (i.e. for different vibrational levels) has shown that, for low values of R, protons move apart preferentially parallel to the axis of the beam. For large values of R, dissociation with the orientation of the internuclear axis at right angles to the axis of the beam is more likely. The simultaneous excitation of the target can markedly alter the distribution and can lead to various anomalies[43,45-48].

The cross-section for the dissociation of H_2^+ ions due to electronic transitions has been estimated theoretically by various investigators in terms of the Born approximation[49-56]. Despite the fact that this is a high-energy approximation, it has been used successfully for energies in the range 1–100 keV. The contribution of the vibrational mechanism to the total dissociation cross-section has also been estimated[57]. For this purpose, the classical momentum approximation was employed[58]. For an energy of H_2^+ ions of 3 keV and collisions with hydrogen atoms, the cross-section for the vibrational dissociation is approximately 10% of the experimental value. Calculations have been made for vibrational transitions due to polarisation forces in terms of a modified Born approximation[59].

Table 1. The dissociation cross-sections Σ of H_2^+ ions obtained from different molecules.

Initial molecule	H_2	CH_4	C_2H_4	C_4H_{10}	$C_{12}H_{24}$	GeH_4	SiH_4
$10^{16} \cdot \Sigma$, cm^2	1.06[65]	2.5[66]	1.4[65]	1.7[65]	1.4[65]	2.1[67]	1.7[67]

The dissociation cross-section of H_2^+ ions depends on vibrational excitation. Experiments confirming this fact have been carried out by different groups of investigators[60-64]. H_2^+ ions were obtained not only by the ionisation of H_2 molecules by electrons of different energies but also in the dissociative ionisation of various hydrogen-containing molecules[65-67]. Table 1 lists the experimental dissociation cross-sections of H_2^+ ions obtained from different molecules. The energy of the H_2^+ ions was 3.8 keV and the target was neon. Evidently the most excited H_2^+ ions are formed in the dissociative ionisation of methane molecules by electrons (E_e = 120 eV).

The interpretation of experiments on the dissociation of N_2^+ is less unambiguous than in the case of H_2^+ owing to the more complicated electronic structure[69-72]. A marked dependence of the impact dissociation cross-section of N_2^+ ions on the energy of the electrons ionising the nitrogen molecules has been observed in a number of studies[73-75]. This result suggests an appreciable proportion of excited N_2^+ ions in the beam. Among these may be not only vibrationally excited but also electronically excited ions. The N_2^+ ions formed by the ionisation of HN_3 molecules are appreciably excited[76]. The most probable process in the dissociation of N_2^+ ions for energies in the region of about

10^3 eV is an electronic transition to a section of the $D^2\Pi_g$ potential curve above the dissociation limit and predissociation in the $C^2\Sigma_u^+$ state[77,78].

Heteronuclear ions dissociate via the same mechanisms as homonuclear ions. However, there are certain characteristic features owing to the presence of a permanent dipole moment in heteronuclear ions[59]. The dissociation of the heteronuclear ions HeH^+,[79-81] HD^+,[82,83] CO^+, and NO^+ [72] has been studied.

IV. METASTABLE IONS

In mass-spectrometry metastable ions are excited ions whose lifetime with respect to decomposition and emission is of the order of 10^{-6}–10^{-5} s. This is determined by the residence time of the ions in the ion source after their formation as a result of the ionisation of the molecules by electrons and by the time taken to traverse the path from the field-free region of the mass-spectrometer to the point where the metastable ion decomposes. The observed slow decompositions of the ions may be due to different causes. Firstly, as a result of the ionisation of the molecule, the ion can be formed in excited electronic states, which have longer lifetimes with respect to emission and emit with transition to an unbound state or to a section of a bound state above the dissociation limit. Secondly, the ion may be in an excited state which has a barrier; in this case the dissociation proceeds via the tunnel effect. Calculations of the permeability of the barrier carried out by the usual equations have shown that, for example, for a barrier height of 1 eV and widths of 0.15 and 0.25 Å, the lifetimes of N_2^{2+} and NO^{2+} are found to be respectively $\sim 10^{-7}$ and 10^{-6} s.[16] Calculations for the spontaneous decomposition of $C_2H_4^{2+}$ and CO^{2+} ions have shown that their lifetimes are of the order of $\sim 10^{-5}$ and 10^{-4} s respectively.

The third possible mechanism involves slow predissociation in the excited state of the ion. Predissociation usually takes place during a period which is much shorter than the lifetime with respect to emission. When not all the selection rules are obeyed, predissociation is then slow[84]. Thus the metastable ion will be observed when the predissociation time is of the order of magnitude of the lifetime with respect to emission, which in turn should be $>10^{-7}$ s.

The rate of predissociation in the mass-spectra of polyatomic molecules, is calculated using the quasiequilibrium theory of mass-spectra, the latest review of which has been written by one of its originators[85]. This theory presupposes that the processes leading to the formation of the mass-spectra consist of a series of consecutive and competing reactions, the rates of which can be calculated on the basis of the theory of absolute reaction rates.

The general expression for the rate constant for a unimolecular reaction is[85]:

$$k(E) = \frac{S}{h}[N^*(E-\varepsilon_0)/\rho(E)],$$

where S is the symmetry factor equal to the number of identical reaction paths (with the same activation energy and activated complex), h Planck constant, $N^*(E-\epsilon_0)$ the number of states of the activated complex with energy $\leq E-\epsilon_0$, $\rho(E)$ the density of the states of the initial ion with a total energy E, and ϵ_0 the activation energy.

The quasiequilibrium theory predicts that the rate constant should be a monotonically increasing function of the internal energy. Considering the molecular ion as an assembly of N harmonic oscillators (N is the number of internal degrees of freedom of the molecular ions) and assuming for simplicity that the frequencies of all the oscillators are identical, we obtain a simple expression for the decomposition rate constant:

$$k(E) = \nu\left(1-\frac{\varepsilon_0}{E}\right)^{N-1},$$

where ν is the frequency factor.

Table 2. C–H bond dissociation energies E_{C-H}.

Ion	$C_3H_8^+$	$C_3H_7^+$	$C_3H_6^+$	$C_3H_5^+$	$C_3H_4^+$	$C_3H_3^+$
E_{C-H}, kcal mole^{-1}	8	92	49	102	44	150

Ions with a large excitation energy E have large decomposition rate constants and decompose in the ion source. Weakly excited ions have $k \simeq 10^6$ s^{-1} and decompose after emerging from the ion source into the field-free region of the analyser, forming "metastable peaks". Since metastable ions are weakly excited, the energy of the process should play a significant role in their dissociation. In particular, one may expect appreciable differences in the spontaneous decomposition of alkane ions with even and odd numbers of hydrogen atoms. Table 2 presents the dissociation energies of the C–H bonds for ions with three carbon atoms[85] and Table 3 lists the intensities of the spontaneous decompositions for the corresponding ions obtained from propane molecules.

Table 3. The intensities of the spontaneous decompositions (% relative to the intensity of the initial ions).

Decomposition process	I^*/I, %	Decomposition process	I^*/I, %
$C_3H_8^+ \rightarrow C_3H_7^+ + H$	1.5	$C_3H_6^+ \rightarrow C_3H_5^+ + H$	0.1
$C_3H_7^+ \rightarrow C_3H_5^+ + H_2$	0.1	$C_3H_5^+ \rightarrow C_3H_3^+ + H_2$	2.0

The last Table shows that the spontaneous decomposition of ions with an even number of hydrogen atoms proceeds with loss of one hydrogen atom in accordance with the low activation energies for this process listed in Table 2. The spontaneous decomposition of ions with an odd number of hydrogen atoms involves the loss of two hydrogen atoms in the form of a molecule, since the activation energy for this process is reduced owing to the formation of a bond between the two hydrogen atoms abstracted.

The significant influence of the energy relations on the dissociation process frequently leads to the decomposition of the metastable ions via pathways other than simple bond dissociation. In particular, many rearranged ions are formed, since the decomposition reactions with the rearrangement of these atoms have small activation energies. This process has been discussed in detail in a monograph[88]. The decomposition of the molecular ion derived from benzoic acid labelled with deuterium in the

carboxy-group may be quoted as an example of the interchange of the positions of the atoms involved in the decomposition of metastable ions. In this case the loss of the OH group is twice as likely as the loss of OD, while for the decomposition in the ionisation chamber during periods comparable to the time required for the rotation of the carboxy-group the loss of OD groups predominates greatly over the loss of OH groups[89].

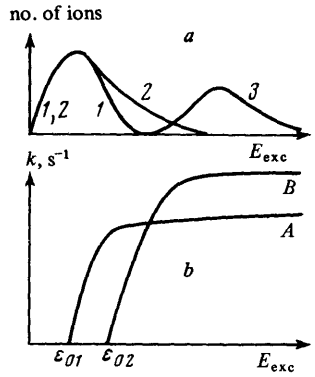

Figure 6. Impact activation of the direct bond dissociation reaction[91].

The contribution of decomposition reactions with rearrangement is greater by 2–3 orders of magnitude compared with simple bond dissociation reactions for metastable ions than for the ions decomposing in the ionisation chamber[90]. The rearrangement reactions hinder the determination of the structure of the metastable ions and their contribution may be reduced by the impact activation of the direct bond dissociation reactions. This idea is illustrated schematically in Fig. 6. Fig. 6*a* shows the distribution of ions with respect to the excitation energy E_{exc} in the ion source at the instant of their formation (curve *2*). Curve *1* describes the distribution with respect to excitation energy of the metastable ions which do not have sufficient time to dissociate in the ion source and decompose in the field-free region. Curve *A* in Fig. 6*b* represents the hypothetical dependence of the decompositon rate constant for rearrangement reactions on the excitation energy E_{exc}. Curve *B* illustrates the analogous relation for the simple bond dissociation rate constant. Curve *A* is below curve *B* for high values of E_{exc}, because the rearrangement reactions have lower frequency factors than the direct bond dissociation reactions. On the other hand, the activation energy $\epsilon_{01} < \epsilon_{02}$. The Figure shows that metastable ions, which have low excitation energies, decompose mainly via rearrangement reactions. In order to reduce their contribution, it is necessary to increase the excitation energy of the metastable ion, i.e. to shift the distribution defined by curve *1* to the position characterised by curve *3*. This is achieved by the collision of the metastable ion with a neutral particle in the region of ion drift. It has been shown[91] for the molecular ions $C_6H_5CD_3^+$ and $C_6D_5CH_3^+$, which decompose with abstraction of H or D atoms, that the contribution of the decomposition with a rearrangement of H and D atoms in impact activation is smaller by a factor of 5 compared with the spontaneous decomposition of the ions.

In the mass-spectra of polyatomic molecules the fraction of metastable ions can be fairly high. It has been shown[32] that in the mass-spectrum of n-octane, 26% of the molecular ions $C_8H_{18}^+$ undergo a metastable transition leading to the formation of the ions $C_6H_{13}^+$. Many instances of the spontaneous decomposition of molecular and fragment ions in the mass-spectra of n-octane, n-hexane, benzene, n-butane, isobutane, and other compounds have been investigated[32,57] with the aid of a double mass-spectrometer. Certain aspects of the spontaneous decomposition of polyatomic ions have been elucidated in a review[92].

We shall also consider the spontaneous decompositions of doubly-charged ions and certain simple singly-charged ions. As in the study of the decomposition of other metastable ions, valuable information is obtained here by studying the energy spectra of the dissociation products.

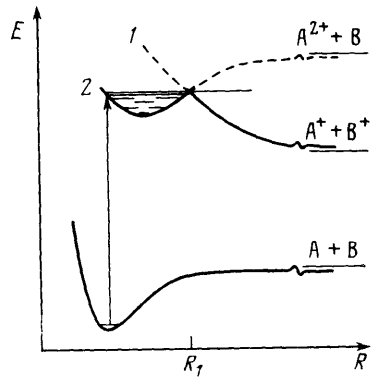

Figure 7. Hypothetical potential energy curves for a doubly-charged ion.

In the decomposition of doubly-charged ions the kinetic energy of the fragments in the centre of mass system is high (several electron-volts) and the peak has a characteristic shape with two vertices and an intervening minimum[93]. The depth of the minimum depends on the width of the collimating slits and the distance between the vertices defines the most probable kinetic energy of the fragments in the centre of mass system. The distance between the charged fragments in the doubly-charged ion can be inferred from this kinetic energy. Fig. 7 presents schematic potential curves for a neutral diatomic molecule and its doubly-charged ion. For large interatomic distances R, the potential energy of the system of ions A^+ and B^+ varies in accordance with the Coulomb law: namely as e^2/R. The overall energy of A^{2+} and B tends to a limit, which lies above the sum of the ionisation potentials of A and B, since the double-ionisation potential of A is greater than the sum of the ionisation potentials of A and B. For a certain value of R_1, the total energies of states *1* and *2* are equal. At this point the states leading to the formation of $A^+ + B^+$ and to $A^{2+} + B$ intersect, provided that they have different symmetries[84]. For the same symmetry and spin, the levels do not intersect, which leads to the formation of a barrier in one of the states. If the AB^{2+} ion is formed in a vibrationally excited state

close to the top of the barrier, then rapid predissociation takes place since the corresponding selection rules are fulfilled[84]. When the AB^{2+} ion is formed in the lower vibrational levels, it is almost stable, since the probability of passing through the barrier decreases sharply with increase of its width and height. The lifetimes characteristic of metastable ions ($\lesssim 10^{-5}$ s) will be observed in a small region of excitation energies of the AB^{2+} ion, located several tens of electron-volts below the top of the barrier. The energy of the A^+ and B^+ fragments in the centre of mass system will thus characterise the position of the top of the barrier.

For the doubly-charged ions N_2^{2+}, O_2^{2+}, I_2^{2+}, Br_2^{2+}, IBr^{2+}, and ICl^2, the kinetic energies of the fragments and the position of the top of the barrier have been determined[94]. The kinetic energy of the fragments from CO^{2+} has been found to be [57,95,96] 5.5– 6 eV, which corresponds to R = 2.6 Å. Metastable decompositions have been observed also for the CO_2^{2+} and N_2O^{2+} ions[96], the $C_2H_4^{2+}$, $C_2H_3^{2+}$, and $C_2H_2^{2+}$ ions[57,97], and for the doubly-charged ions derived from aromatic hydrocarbons (benzene, naphthalene, and biphenyl derivatives)[98]. The ion decomposition reaction $C_6H_6^{2+} \rightarrow CH_3^+ + C_5H_3^+$ results in the liberation of 2.8 eV of energy, which corresponds to a charge separation in the ion of 5.14 Å.[99]

Metastable ions were observed recently for the diatomic single-charged ions N_2^+ and NO^+ [16,17,100,101] and HS^+ ions[102]. The predissociated states were not identified exactly and much work is still required here.

V. IMPACT DISSOCIATION OF POLYATOMIC IONS

Systematic studies have been made on a double mass-spectrometer (Fig. 2) of the dissociation of a series of polyatomic ions on collision with various targets[57]. The total cross-sections for dissociation via different channels (reaching values of about 4×10^{-15} cm^2 for certain ions), their dependence on the excitation energy of the initial ion and its origin, and the dependence of the cross-sections on the kinetic energy of the ions and the type of target have been determined. Such data have been obtained for the ions[10–14,32,57] CH_4^+, CD_4^+, CH_5^+, CD_5^+, $C_2H_4^+$, $C_2H_4^{2+}$, $C_3H_8^+$, $C_4H_{10}^+$, $C_6H_6^+$, $C_7H_{16}^+$, $C_8H_{18}^+$, and many others[57]. Comparison of the mass-spectra of molecules in dissociative ionisation by electrons with the dissociation spectra of the corresponding ions obtained on collision between the accelerated molecular ions and neutral particles is also of interest.

1. Dependence of the Total Dissociation Cross-Sections and the Dissociation Spectra on the Dissociation Energy of the Ions and the Type of Target

Table 4 presents the dissociation spectra of ions from methane obtained when they collide with different atoms and molecules[10,12,57]. The kinetic energy of the ions was 2530 eV and the energy of the electrons in the ion source was 70 eV.

The Table shows that the dissociation spectra depend only slightly on the mass and the structure of the neutral target particle‡. However, the absolute values of the cross-sections differ markedly. For example, the cross-section for the process $CH_4^+ \rightarrow CH_3^+ + H$ on collision of CH_4^+ ions with air molecules is 7×10^{-16} cm^2, while on collision with hydrogen it amounts to only 2.5×10^{-16} cm^2. Similar results were obtained for the dissociation of ions from ethylene in collisions with air molecules and neon atoms[103].

‡Only collision with helium leads to more extensive dissociation.

Table 4. The relative intensities of the products of the dissociation of methane ions on collision with the target atoms and molecules.

Process		Target						
		He	Ne	Ar	H_2	n-C_4H_{10}	n-C_5H_{12}	CH_4
CH_4^+	$\rightarrow CH_3^+$	100	100	100	100	100	100	100
	$\rightarrow CH_2^+$	53	44	49	50	34	35	39
	$\rightarrow CH^+$	17	9	11	11	9	10	9
	$\rightarrow C^+$	6	3	4	4	3	3	3

The cross-sections for the individual processes depend to a large extent on the energy consumed in the process. Table 4 shows that the cross-sections decrease appreciably with increase of the number of hydrogen atoms lost, which also requires greater energy expenditure. However, for high energies of the ions, the cross-sections for the individual processes approach one another[13]. This may be associated with the increase of the excitation energy received by the ion in the collision and also with the increase of the contribution to the dissociation cross-section by processes involving the loss ("abstraction") of an electron, which results in the simultaneous dissociation of several bonds in the case of methane.

Table 5. The dissociation cross-sections ($10^{16}\sigma$, cm^2) of CD_5^+ ions on collision with air molecules and neon atoms.

Decompositon process		ϵ_0, eV	Neon	Air
CD_5^+	$\rightarrow CD_4^+ + D$	4.4	0.13	0.28
	$\rightarrow CD_3^+ + D_2$	1.3	1.1	2.0
	$\rightarrow CD_2^+ + D_2 + D$	6.5	0.3	0.56
	$\rightarrow CD^+ + 2D_2$	5.5	0.08	0.18
	$\rightarrow C^+ + 2D_2 + D$	9.3	0.03	0.06
Total cross-section Σ			1.64	3.06

A dependence of the cross-section on the energy ϵ_0 consumed in the given dissociation process has been observed for all the processes studied with the kinetic energies of the initial ions in the region of several keV. Table 5 illustrates this fact for the CD_5^+ ions obtained in the ion source by an ion–molecule reaction.

It is interesting to note[57] that the total dissociation cross-section of CD_5^+ ions is smaller almost by a factor of two than for CD_4^+ ions. On the basis of the relation between the dissociation cross-section and the process energetics, this can be accounted for by the greater stability of the CD_5^+ ion compared with the CD_4^+ ion. The greater stability of CD_5^+ may be due to the structure of its electron shell, which is isoelectronic with that of the neon

atom, and the low internal excitation energy, which, as will be seen from the description below, greatly influences the total dissociation cross-section. Other examples of this kind can be found in studies on the dissociation of ions produced from propane as a result of collision with neon atoms. Table 6 lists the cross-section for the formation of dissociation products with three, two, and one carbon atoms and the total dissociation cross-sections Σ of certain ions from propane with a kinetic energy of 2.8 keV.[57,105]

Table 6. The overall dissociation cross-sections of the ions formed from propane ($10^{16}\sigma$, cm^2).

Dissociation products	Initial ions							
	$C_3H_8^+$	$C_3H_7^+$	$C_3H_6^+$	$C_3H_5^+$	$C_3H_4^+$	$C_3H_3^+$	$C_3H_2^+$	C_3H^+
$C_3H_n^+$	6.2	5.3	7.6	5.7	7.5	4.2	3.9	2.1
$C_2H_m^+$	13.6	3.1	1.8	0.7	0.4	0.3	0.4	0.4
CH_k^+	0.5	0.4	0.3	—	—	—	—	0.6
Σ	20.3	8.8	9.7	6.4	7.9	4.5	4.3	3.1

Evidently, with decrease of the number of hydrogen atoms in the initial ion, the cross-section for dissociation with rupture of the C–C bond decreases rapidly, becoming constant starting with the $C_3H_4^+$ ion. This behaviour reflects the fact that, with decrease of the number of hydrogen atoms in the ions, the C–C bond is stabilised up to the formation of a double bond in the $C_3H_4^+$ ion. The structure of the $C_3H_8^+$ ion is particularly unstable owing to the greatly weakened C–C bond. The abstraction of a single hydrogen atom leads to a sharp alteration of the structure and the formation of the protonated cyclopropane ring in the $C_3H_7^+$ ion, which is stable. Ions with a smaller number of hydrogen atoms probably retain this carbon skeleton with a gradual increase in the strength of the C–C bonds in the ring. The variation of the total dissociation cross-sections of these ions reflects the variation of the overall cross-sections for the abstraction of hydrogen atoms, which are somewhat greater for ions with an even number of hydrogen atoms (an odd number of electrons), Such variation of the cross-sections with abstraction of hydrogen atoms is characteristic of the ions in the mass-spectra of saturated hydrocarbons and implies that the strength of the C–H bonds varies depending on whether the number of hydrogen atoms in the ion is even or odd.

Spontaneous decomposition processes, superimposed on impact dissociation, have been observed for polyatomic ions[32,106]. As a rule, a high cross-section for dissociation on collision corresponds to an intense spontaneous decomposition of the ions, which is related to the influence of the initial excitation energy of the dissociation cross-section. Many characteristics of the impact dissociation of the ions in the mass-spectrum of n-butane and other molecules have been examined[57,107].

The total cross-sections for the dissociation, with the rupture of C–C bonds, of the molecular ions from saturated hydrocarbons are additive, i.e. the cross-section is proportional to the number of CH_2 groups in the initial ion[32,57]; the data in Table 7 illustrates this finding.

2. Comparison of the Impact Dissociation Spectra of Ions with the Mass Spectra of Molecules Obtained on Electron Impact

Comparison of the dissociation spectra of ions with their mass spectra obtained on electron impact is of great interest. Such a comparison is presented in Tables 8 and 9 for the $C_3H_8^+$ and $C_3H_3N^+$ ions and the corresponding molecules[57,103].

Table 7*. Total dissociation cross-sections Σ (Kupriyanov[57]).

Initial ion	$C_3H_{10}^+$	$C_3H_{14}^+$	$C_4H_{10}^+$	$C_4H_8^+$
$10^{15}\cdot\Sigma$ (calc.), cm^2	4.0	3.0	2.0	1.5
$10^{15}\cdot\Sigma$ (expt.), cm^2	$4.3^{\pm 3}$	$3.0^{\pm 3}$	$2.3^{\pm 6}$	$1.4^{\pm 7}$

*In the calculation of Σ it was assumed that the contribution to the total decomposition cross-section by one CH_2 group in the molecular ion is 5×10^{-16} cm^2.

The mass-spectra of the molecules were obtained for an electron energy of 70 eV. The energy of the accelerated ions was 3.5 keV and the dissociation occurred on collision with air molecules.

Table 8. Comparison of the mass-spectrum ($I_{m.s.}$) of propane and the impact dissociation spectrum (I_{im}) of the propane ion (the relative intensities of the fragment ions are quoted).

Ions	$C_3H_7^+$	$C_3H_6^+$	$C_3H_5^+$	$C_3H_4^+$	$C_3H_3^+$	$C_3H_2^+$	C_3H^+
$I_{m.s.}$	8.7	3.9	7.4	1.5	23.0	23.5	13.5
I_{im}	17.4	2.8	5.4	1.2	22.8	23.5	16.7

Table 9. Comparison of the mass-spectrum of C_3H_2N molecules ($I_{m.s.}$) and the impact dissociation spectrum (I_{im}) of $C_3H_2N^+$ ions (the relative intensities of the initial and fragment ions are quoted).

Ions	$C_3H_2N^+$	C_3HN^+	C_3N^+	C_3N^+ $C_3H_3^+$	C_3H^+	$C_3H_3^+$ CNH+	$C_3H_2^+$ CN+	C_3H^+
$I_{m.s.}$	29.5	12.6	3.2	2.6	1.7	7.1	39.4	3.9
I_{im}	36.0	12.2	1.3	3.4	1.4	6.3	36.2	3.2

A comparison of the impact dissociation spectra with the electron impact mass-spectra has also been made for a whole series of other molecular ions (derived from methane, ammonia, water, ethylene, n-octane, n-hexane, benzene, etc.). A significant similarity between the impact dissociation spectra of the ions with an energy of about 3–4 keV and the mass-spectra of the corresponding molecules follows from the data in Tables 8–10 and the

results published by Kupriyanov[57]. A similar phenomenon was noted also by other investigators[28]. Table 10 presents a section of the dissociation spectrum of benzene ions $C_6H_6^+$ and the corresponding section of the mass-spectrum of benzene itself[108]. The mass-spectrum was recorded for an electron energy of 70 eV. The kinetic energy of the $C_6H_6^+$ ions was 8 keV.

Table 10. Comparison of the mass-spectrum ($I_{m.s.}$) of benzene and the impact dissociation spectrum (I_{im}) of benzene ions (the relative intensities of the fragment ions are quoted).

m/e	68	67	66	65	64	63	62	61	55	54	50	40	39
$I_{m.s.}$	43	100	67	46	51	45	25	13	11	18	57	90	92
I_{im}	44	100	57	45	46	36	21	8	11	20	67	117	86

The similarity of the dissociation spectra and the mass-spectra has been noted in the literature for a whole series of other aromatic compounds. It has been shown[57] that the impact dissociation spectra of the $C_3H_6^+$ and $C_4H_8^+$ ions obtained by the ionisation of various molecules are not only close to one another, as can be seen from the data in Table 11, but they also resemble the mass-spectra of the corresponding C_3H_6 and C_4H_8 molecules.

Table 11*. Comparison of the mass-spectra of molecules and the impact dissociation spectra of ions obtained from different compounds.

Process	Dissociation spectra: Initial molecule C_3H_6	C_4H_{10}	C_6H_{14}	Mass-spectra: a	C_3H_6	b
$C_3H_6^+ \rightarrow C_2H_m^+$	85	83	78	81		76
$C_3H_6^+ \rightarrow CH_k^+$	15	17	22	19		24

Process	Initial molecule C_4H_{10}	C_6H_{14}	C_8H_{18}	c	C_4H_8	d
$C_4H_8^+ \rightarrow C_3H_n^+$	69	54	50	60		58
$C_4H_8^+ \rightarrow C_2H_m^+$	29	43	46	38		40
$C_4H_8^+ \rightarrow CH_k^+$	2	3	4	2		2

* The overall intensities were assumed to be 100.
a) Propene; *b*) cyclopropane; *c*) *cis*-but-2-ene; *d*) *trans*-but-2-ene; energy of the ions 3 keV; target—neon.

Such similarity of the mass-spectra of the ions suggests that in both cases, i.e. in impact dissociation of the ion and in the ionisation of the corresponding molecule by electrons, approximately identical excited ions are produced[109]; the mechanism of their dissociation is also the same.

The similarity of the mass-spectra has likewise been noted in other ion-formation processes, particularly in charge-transfer processes[110,111]. This problem has been examined in detail[112]. In all these instances the energy of the ions does not exceed several keV. For higher kinetic energies of the ions (about 20 keV and above), an appreciable difference is observed between the dissociation spectra of the ions and the mass-spectra of the corresponding molecules. This has been demonstrated for the dissociation of CH_4^+ ions[13,57,103], $C_2H_4^+$ ions,[103] and a number of other ions[13,57]. In these cases, the collisions of the ions with atoms and molecules lead to strong excitation of the ions, as a result of which they dissociate with abstraction of many hydrogen atoms (in the case of CH_4^+ ions) with the same probability as the dissociation involving the abstraction of a single hydrogen atom[13,57,103]. Therefore one should note that an increase of electron energy up to 12 keV does not lead to an intense decomposition of CH_4 molecules under electron impact of the kind observed for the dissociation of CH_4^+ ions on collision with heavy particles in the range of energies of the order of tens of kiloelectron-volts[114].

3. Characteristics of the Ion Dissociation Spectra

Table 12 shows that for each energy there are identical regions in the dissociation spectra of the initial ions containing different numbers of hydrogen atoms. This phenomenon, which we called the "inclusion" of the dissociation spectra of ions[114,115], occurs also for NH_3^+ and NH_2^+ ions[13] as well as certain other ions[57].

Table 12. Parameters of the dissociation spectra of various ions derived from methane for several (four) collision energies (the cross-section for the formation of the C^+ ion was assumed to be 1.0).

Dissociation products	Initial ions: CH_4^+	CH_3^+	CH_2^+	CH_4^+	CH_3^+	CH_2^+
	E_0=1350 eV (Ref.12)			E_0=3000 eV (Ref.12)		
CH_2^+	21	20	—	11	12	—
CH^+	4	5	4	3	4	3
C^+	1.0	1.0	1.0	1.0	1.0	1.0
	E_0=30 keV (Ref.13)			E_0=90 keV (Ref.13)		
CH_2^+	1.9	2.0	—	1.2	1.3	—
CH^+	1.3	1.3	1.3	1.0	1.0	1.0
C^+	1.0	1.0	1.0	1.0	1.0	1.0

Table 13 shows that the phenomenon of "inclusion" of the dissociation spectra is observed for the majority of processes. Thus the situation arises in which the dissociation spectra of ions containing a larger number of hydrogen atoms include the dissociation spectra of ions with a smaller number of hydrogen atoms.

The "inclusion" of spectra makes it possible to infer from the known mass-spectra of molecules obtained on electron impact the mass-spectra of radicals, which are as a rule unknown. In fact, since the spectra for dissociation on collision with molecules and the mass-spectra of molecules under electron impact are similar, presumably the phenomenon of "inclusion" will be observed also for neutral molecules. Table 14 presents the mass-spectra of methane and the radicals CH_3, CH_2, and CH calculated[57,115] from the methane mass-spectrum (b) and

determined experimentally[116] (a). Column c presents the parameters of the mass-spectra calculated from the mass-spectrum for CH_3 radicals.

Table 13. Parameters of the dissociation spectra of the ions obtained from propane (the cross-section for the formation of the CH_3^+ ion was taken to be 1.0).

Dissociation products	Initial ions					
	$C_3H_8^+$	$C_3H_7^+$	$C_3H_6^+$	$C_3H_5^+$	$C_3H_4^+$	$C_3H_3^+$
$C_3H_6^+$	5.2	5.9	—	—	—	—
$C_3H_5^+$	12.8	22.0	10.6	—	—	—
$C_3H_4^+$	2.4	2.3	3.9	0.7	—	—
$C_3H_3^+$	10.5	11.1	10.6	10.5	7.1	—
$C_3H_2^+$	1.9	1.8	2.0	1.9	2.0	1.3
C_3H^+	1.0	1.0	1.0	1.0	1.0	1.0

Table 14 shows that the mass-spectra of CH_3 radicals determined experimentally[116] and calculated[57,115] from the methane mass-spectrum agree satisfactorily. There are no experimental data for the mass-spectra of CH_2 and CH radicals. However, their calculated mass-spectra also agree with the dissociation spectra of CH_3^+ and CH_2^+ ions as well as the dissociation spectra of CH_4^+ and CH_3^+ ions. Therefore one may suppose that the experimental mass-spectra of the radicals are close to those whose parameters are listed in Table 14. Further experimental studies are necessary in order to extend this rule to the mass-spectra of other radicals.

Table 14. Parameters of the mass-spectra of methane and certain radicals (the relative cross-sections are expressed in arbitrary units).

Ions formed	Species ionised						
	CH_4	CH_3		CH_2		CH	
		a	*b*	*b*	*c*	*b*	*c*
CH_3^+	31	28	31	—	—	—	—
CH_2^+	6	9	6	6	9	—	—
CH^+	3	3	3	3	3	3	3
C^+	1	1	1	1	1	1	1

4. Dependence of the Ion Dissociation Cross-sections and Spectra on the Electron Energy and the Origin of the Ions

The impact dissociation cross-sections of polyatomic ions as well as those of diatomic ions increase with increase of the electron energy until the attainment of constant values. Fig. 8 illustrates the variation of the dissociation cross-section with electron energy in the ion source for $C_2H_3^+$ ions, which decompose via different channels[114]. The ion energy was 2.8 keV. The corresponding relations for other ions derived from ethylene and methane have also been examined[57,117].

Markedly different impact dissociation cross-sections were obtained for the dissociation of diatomic ions of different origins[65,76], which suggests an appreciable difference between the distributions with respect to excited states for identical ions from different molecules (see Section III). For polyatomic ions, the dissociation cross-sections of identical ions of different origins differ from one another to a lesser extent[10,118]. For example the dissociation cross-sections of the CH_3^+ ions obtained from CH_4 and n-butane are similar[10] and this is also true of the $C_2H_4^+$ ions obtained from C_2H_4, C_3H_8, and n-C_4H_{10}.[118] It is noteworthy that the internal excitation energy in a polyatomic ion can affect not only the total dissociation cross-section, as in a diatomic ion, but also the dissociation spectrum. It is seen from Fig. 8 that the total dissociation cross-section varies mainly as a result of the increase of the cross-section for dissociation processes with a low activation energy. The internal excitation energy has only a slight influence on the cross-sections for dissociation processes with a high activation energy. In order to achieve such processes, the initial ion must be strongly excited on collision and, in conformity with the considerations put forward in Section IV and the discussion of Fig. 6, such a highly excited ion will decompose mainly as a result of simple bond dissociation.

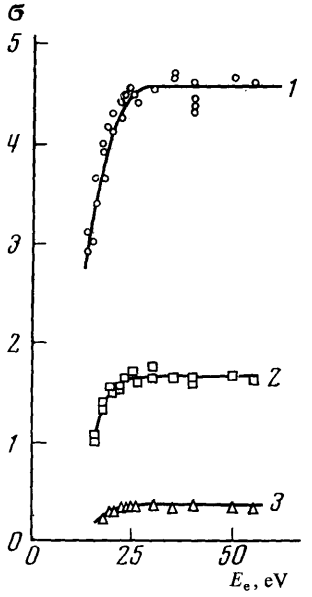

Figure 8. Effect of the electron energy E_e on the relative impact dissociation cross-sections of $C_2H_3^+$ ions: 1) $C_2H_3^+ \rightarrow C_2H_2^+$; 2) $C_2H_3^+ \rightarrow C_2H^+$; 3) $C_2H_3^+ \rightarrow C_2^+$.

Thus the relative yield of the fragments whose formation requires high energies will not depend markedly on the initial excitation energy but will be determined mainly by the structure of the initial ion. The differences between the dissociation spectra in the region of such fragments for identical ions of different origins indicate differences between the structures of these ions. This conclusion has been reached[119] on the basis of an analysis of the dissociation spectra of the $C_6H_7^+$ ions from cyclohexa-1,4-diene and methylcyclohexa-1,4-diene.

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Much less can be said about the specific mechanisms of the impact dissociation of accelerated polyatomic ions than about the dissociation of diatomic ions owing to the insufficiency of detailed information about the decomposition of polyatomic ions, which can be obtained from the angular and energy distributions of the fragments. In the general case the dissociation process can be divided into two stages. Initially, at the instant of collision between the accelerated ion and the target particle, the electronic and vibrational degrees of freedom of the ion are excited. The order of magnitude of the collision time τ is defined by the relation $\tau = \sqrt{\Sigma}/v_0$, where Σ is the total dissociation cross-section.

For the energies of the initial ions $E_0 \simeq 10^3$ eV, τ is approximately 10^{-15}–10^{-16} s. On the other hand, the time of the most rapid dissociation is 10^{-13} s. Therefore in the second stage the isolated molecular ion excited by collision decomposes in accordance with the quasiequilibrium theory of mass-spectra.

The principal experimental characteristics of the impact dissociation of polyatomic ions can be briefly generalised by the following postulates:

1. The dissociation spectra of polyatomic ions depends only slightly on the nature of the neutral target. They are determined by the structure and energy of the excited ions and also by their kinetic energy.
2. The dissociation spectrum is independent of the electron energy in the ion source for $E_e \geqslant 30$ eV. The excitation of the initial molecular ion greatly affects dissociation processes with a low activation energy and only weakly influences dissociation processes with a high activation energy.
3. The total dissociation cross-section depends on the ion dissociation energy. The more stable the given structure the smaller the total dissociation cross-section of the given ion, other conditions being equal.
4. For many ions derived from saturated hydrocarbons, the total cross-section is an additive function of the number of CH_2 groups in the ion.
5. The impact dissociation spectra of the ions and the mass-spectra of the corresponding molecules under electron impact are similar under certain conditions.
6. Similar dissociation spectra have been obtained for many ions differing from one another only in the number of hydrogen atoms (the "inclusion" of the spectra).
7. The decomposition of ions via different channels proceeds with similar probabilities for higher kinetic energies of the ions.

On the basis of these empirical characteristics, it is possible to reach conclusions, admittedly so far qualitative, about the differences or similarities between the structures of ions of identical composition obtained in different ionisation processes. Examples of this kind for the $C_3H_6^+$ ions from cyclopropane and propene and the $C_4H_{10}^+$ ions from n-butane and isobutane can be found in Kupriyanov's thesis[57] and those for the $C_3H_7^+$ ions from different compounds are quoted by Haddon and McLafferty[120]. Table 15 compares the dissociation spectra of the molecular ions from n-butane and isobutane[57].

Evidently these spectra differ markedly for both spontaneous and impact dissociation. This suggests that the structures and excitation energies of the $C_4H_{10}^+$ ions obtained by the ionisation of n-butane and isobutane molecules are different. It is noteworthy that further investigation and accumulation of experimental data are necessary to refine the characteristics of the impact and spontaneous dissociation of polyatomic ions. In particular, the problem of the individual influence of the excitation energy and structure of the ions on their total dissociation cross-section and dissociation spectrum is of interest. The results available at present suggest that the excitation energy probably affects the total dissociation cross-section to a greater extent, while the structure has a greater influence on the dissociation spectrum of the ions. Under real experimental conditions, the beam of the initial ions may contain ions with different structures and excitation energies and the observed differences in the impact dissociation pattern of such ions reflect the differences in the distribution of the initial ions with respect to structure and excitation energy. More careful experiments with allowance for the above factor are needed to solve this problem. In this sense mass-spectrometric study of the photodissociation of ions formed by the photoionisation of molecules with simultaneous analysis of the dissociation products with respect to the angle at which they are ejected and the kinetic energies is promising.

Table 15*. Parameters of the dissociation spectra of the ions obtained from n-butane and isobutane (relative cross-sections).

Decomposition process	n-Butane		Isobutane	
	a	*b*	*a*	*b*
$C_4H_{10}^+ \rightarrow C_3H_7^+$	0.9	9.5	0.1	6.3
$C_4H_{10}^+ \rightarrow C_3H_6^+$	0.9	2.4	0.9	7.5
$C_4H_{10}^+ \rightarrow C_3H_5^+$	0	1.3	0	2.0

* *a*) Spontaneous decomposition spectrum; *b*) impact dissociation spectrum for an ion energy of 3.0 keV; target—air.

The study of spontaneous, induced, and impact dissociation of ions may be called, by analogy with the mass-spectrometry of molecules, the mass-spectrometry of ions if one understands by this the employment of mass-spectrometric techniques for the measurement of the masses and intensities of the ions formed and for the analysis of the structures and excitation energies of the ions obtained in different processes and from different compounds. Thus mass-spectrometry of ions is a new method for the analysis of their structures and excitation energies. It can be used to measure the mass-spectra of ions (by a procedure similar to the measurement of the mass-spectra of molecules), the ionisation potentials and dissociation energies of ions, and other characteristics.

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Effect of An Electric Field on the Thermal Decomposition of Solids

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Studies on the thermal decomposition of solids subjected to the influence of an electric field (EF) are analysed and the effect of the electric field on the rate of decomposition is considered. Attention is drawn to the likely usefulness of the electric field in the study and control of the rates of the thermal decomposition of solids.
The bibliography includes 182 references.

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I. INTRODUCTION

Advances in solid state chemistry (SSC) depend in many ways[1] on the extent of which the theory and experimental techniques of solid state physics (SSP) have been applied to it. The principal difficulty here is associated with the specific features of the problems in solid state physics and chemistry, which require not only a systematic treatment but also an analysis of the achievements of physics in relation to problems in solid state chemistry. This review is devoted to a partial solution of this problem: the analysis and systematic treatment of the scope of the applications of the electric field (EF) as a research technique and a method for controlling the rate of the thermal decomposition of solids. We neglect the magnetic component of alternating electric fields, since it is too small to influence significantly the physicochemical processes in solids.

II. EXAMPLES OF THE EFFECT OF AN ELECTRIC FIELD ON THE DECOMPOSITION OF SOLIDS

The paper of Bel'kevich and Osinovik[2] is apparently the first publication concerning a study of the thermal decomposition of solids in an electric field. The authors investigated by a volumetric method the thermal decomposition of silver oxalate *in vacuo* in the temperature range 105 to 120°C. The specimens were prepared by pressing and were clamped between metallic electrodes. Although the strength of the steady electric field was low (of the order of 3–4 V cm^{-1}) a clear effect of the field on the decomposition process was observed. In the absence of the field the specimens did not explode after attaining the maximum rate of decomposition in the given temperature range, while in the presence of the field an explosion generally occurred. The authors believe that the explosion is not associated with the electric breakdown of the specimens at the instant of the mutual approach of the silver particles, although this does appear to be most likely. The present authors also investigated[3,4] the thermal decomposition of silver oxalate in a constant 80 V cm^{-1} electric field. Three series of experiments were performed: decomposition in the absence of a field; decomposition in a steady field, and decomposition in a periodically applied field. The specimens were heated continuously at a rate of 0.5 deg min^{-1} to 90°C in a vaccum of 10^{-3}–10^{-4} torr. The cell was then disconnected from the pumps, heating was continued, and the amount of carbon dioxide formed before the detonation of the specimen was measured. During the decomposition in the absence of a field, the specimens exploded at 143°C, in a periodically applied field the detonation occurred at 130°C, and in a constant field it occurred at 122°C. Thus the field accelerated the attainment of the maximum rate of thermal decomposition of the specimen at which silver oxalate exploded. Simple calculation of the heat of decomposition rules out the explanation of the observed phenomenon as due to the heating of the specimen by the current.

Bowden and coworkers[5,6] investigated the behaviour of silver azide single crystals between -100° and 50°C in steady and alternating electric fields. At room temperature in a steady electric field weaker than 250 V cm^{-1} the crystals clamped between silver electrodes did not explode, while in higher fields detonation was observed. Before the detonation the resistance of the specimens fell sharply to 10^4 Ω and the crystals exploded approximately 45 s afterwards. The field strength necessary for the explosion of silver azide increased appreciably with decrease of temperature. Thus, whereas at 50°C 19 V was needed for explosion, at -45°C 125 V was already required and at -100°C more than 400 V had to be applied. Calculations showed that approximately 10^{15} electrons per second entered the crystals before detonation and that this was sufficient to heat them to the detonation temperature. It was established that the decrease of the resistence of the crystals before detonation is not caused by the formation of silver dendrites penetrating the crystal. It was suggested that the decrease of the resistance and the detonation of silver azide are due to the injection of electrons from the electrodes in the presence of an electric field. It was also stated[6] that similar results were obtained by Evans and Yoffe for copper azide, and by Berthold for silver acetylide. Subsequently Savel'ev and coworkers[7–9] established that a steady electric field accelerates the thermal decomposition of silver, lead, and barium azides and of silver oxalate. Studies of the effect of the electric field on the rate of thermal decomposition of azides confirmed the conclusion reached earlier using the method of homophase additives. The electric field influenced only the induction period in the decomposition of silver oxalate.

Sukhushin et al.[10] investigated the behaviour of lead, silver, and thallium azides in a strong steady and a pulsed electric field. The azides were found to decompose in the electric field with formation of gaseous and solid products, which was explained by a discrete development of electron avalanches and their chemical effect. Related results were obtained in a study[11] where an unexpected phenomenon,

hindering the investigation of the ferroelectric properties of potassium nitrate in a constant electric field, was observed: after the application of a 1 kV cm^{-1} electric field, a 1 V e.m.f. appeared between the platinum electrodes, which slowly decreased with time and did not disappear even after the specimens had been short-circuited. It was suggested that the phenomenon is caused by the partial decomposition of potassium nitrate in the electric field into potassium ions, nitrogen dioxide, and molecular oxygen with formation of an electrochemical battery. Kabanov and Zharova[12] studied the thermal decomposition of $KMnO_4$ at 220°C in a constant 250 V cm^{-1} electric field and in the absence of a field. The electric field was applied periodically (for 15 s at 5 min intervals) throughout the entire decomposition period. The maximum rate of decomposition of $KMnO_4$ was reached at 54% decomposition in the absence of a field and at 64% decomposition of the preparation under the influence of the electric field. The rate of decomposition of $KMnO_4$ was influenced by the electric field in different ways during different periods. During the first 25 min, the electric field did not affect the rate of decomposition at all, but afterwards the thermal decomposition was accelerated. In the range between 50 and 70 min from the start of the decomposition the electric field stabilised the rate. In the absence of the field there was a smooth increase of the rate of decomposition up to the maximum.

The studies examined above indicate the possibility of a marked influence of the electric field on the decomposition of solids. A common disadvantage of the published investigations is their superficiality, the main aim being to establish merely that an electric field affects the rate of thermal decomposition and yet they permit the conclusion that this rate can be controlled with the aid of the electric field. To develop further and extend studies of this kind, it is necessary to analyse the possible ways in which the electric field influences the rate of thermal decomposition and a systematic treatment of the achievements of solid state physics in this field with an indication of the scope of their applications to solid state chemistry is needed.

III. WAYS IN WHICH AN ELECTRIC FIELD INFLUENCES THE RATE OF DECOMPOSITION OF SOLIDS

The rate of thermal decomposition of solids is greatly influenced[13,14] by point and linear defects and also by the composition of the atmosphere. On the other hand, they give rise to many physical and physicochemical phenomena, which constitutes the basis for considering the ways of which the electric field influences the rate of thermal decomposition solids.

1. Properties of Crystals Grown in an Electric Field

The structure and habit of crystals play[13] a major role in the kinetics of their thermal decomposition. Therefore, by altering the conditions governing the formation of the crystals, it is possible to alter the rate of their thermal decomposition. The study of the influence of the electric and magnetic fields on various physicochemical properties of growing crystals is receiving increasing attention[15–17], since this method of controlling the properties of crystals is more convenient than the method based on the introduction of impurities during crystallisation. It has been established that the electric field has a significant influence on the formation of crystal nuclei and on crystallisation kinetics. Although the problem has been little studied, it is possible to distinguish three possible ways in which the electric field influences the formation of crystals: 1. By the alteration of the properties of water[18–21] (in growing crystals from aqueous solutions) under the influence of a variable electric field in combination with its magnetic component. 2. By the effect of the electric field on the habit and structure of the crystals formed[22–35]. 3. By the electric field[20] initiating a chemical reaction between the solvent and solute, which leads to the entrainment of various impurities by the growing crystals.

The contactless method of applying an electric field to solutions (via glass, air, etc.) is more popular[21,23] than the contact method. It yields more reproducible properties of the grown crystals. When an electric field is applied to the test substances, various types of polarisation arise in the prenuclear groups of atoms: electronic, ionic, and dipole-orientation. The orientation of polar molecules in the field does not occur instantaneously, which promotes the formation of crystals with polar species. In an electric field the number of crystallisation centres initially increases rapidly and then the growth slows down and finally stops completely, reaching saturation. The orienting effect of the electric field frequently entails structural changes in the solvent, which makes it more difficult to understand the mechanism of the influence of the field on the crystallisation process. The nature of the changes in the rate of formation of crystallisation centres under the influence of a variable field depends on temperature[23].

Melent'ev and Kozlovskii[24] studied the effect of an electric field on the crystallisation of lead sulphide from the gas phase. Lead sulphide was vaporised at 850–900°C and, after precipitation on a quartz support, crystallised in a steady electric field. A 2–3 kV cm^{-1} field influences significantly the habit and properties of the growing crystals. For example, Mohs' hardness of the crystals is appreciably lower for specimens grown in the absence of a field; this is associated with the influence of the electric field on dislocation density. Steady and alternating electric fields in supercooled betol, salol, and piperine melts lower[25] the temperature of the onset of crystallisation. The rate of migration of the layers in spiral-laminar crystal growth[26,27] from the gas phase can increase in a steady electric field, which affects the density of the dislocations produced. A change in the structure and catalytic properties of Cu_2O formed in an electric field at 1040°C was observed by Stadnik and Kuznetsov[28], who explained it by the formation of an interstitial solid solution with an excess of copper ions or oxygen.

The influence of an electric field on the crystallisation of amorphous selenium has been observed[29–35] and a number of interesting facts have been established. Thus Geller et al.[29] noted that electric fields up to 10 kV cm^{-1} at mains frequency increase the number of spherolites at 50 to 90°C in selenium specimens with an admixture of bromine and accelerate their growth due to the polarising effect of the electric field on selenium molecules. In a 180 to 360 V cm^{-1} steady electric field the rate of crystallisation of selenium usually[30,31] increases and in higher fields begins to decrease. The growth of spherolites[32,33] under the influence of the electric field takes place usually (but not always) along the lines of force of the field, since the direction of growth depends on the material of the support. On a mica support preferential growth of spherolites in opposition to the lines of force of the electric field is observed, while on a carbon support the growth takes place along the lines of force. A similar result was obtained by Odobescu[34], who investigated the influence of a constant electric field on the kinetics of the crystallisation of selenium from the amorphous and liquid states in the temperature range 150–190°C. He established that the rate of crystallisation of selenium depends

on the direction of the electric field, which exhibits an orienting effect and facilitates the crystallisation process. Bolotova et al.[35] observed the effect of the exposure of liquid selenium to an electric field on its subsequent crystallisation. On cooling in air melts which were not in an electric field, crystals of selenium were not observed.

2. Effect of an Electric Field on Electronic and Ionic Processes

The thermal decomposition of solids is accompanied by different[1,13,14,36,37] electronic processes: the excitation of ions with formation of excitons, polarons, or free electrons and the migration of the local excitation of the crystal with charge transfer, or with energy transfer alone, or with recombination of the excited electrons, which can lead to luminescence in self-activating systems[38]. Apart from luminescence, the above processes give rise also to other physical phenomena: a change in the electronic and hole conductivity[1,12–14,36,37–39], a change in the concentration of the colour centres[13,14], and a change in magnetic properties[40]. Chemical transformations of the initial substances involving the dissociation of old and the formation of new chemical bonds take place simultaneously with physical processes, which implies[41] a redistribution of charges, the transition of electrons from one state to another, or quantum-mechanical resonance.

A common method for altering the concentration of free electrons in the surface region of crystals is that of heterophase additives, the influence of which is explained[42,43] by the transfer of electrons into the substance with a higher work function. We believe[44] that at least two other evident possibilities have been neglected here; chemical interaction of the additive with the substance undergoing decomposition and the influence of the solid decomposition products of the initial substance on the catalytic activity of the additive. As in the method of heterophase additives, the electric field alters the concentration of free electrons in the surface region without changing the structure of the solids. We shall analyse examples of the influence of the electric field on various physical phenomena, which depend on point (in the given case electronic) defects. (The influence of the field on luminescence will be analysed separately).

A strong electric field can alter the state of solids[40] from antiferromagnetic to ferromagnetic by generating conduction electrons. This method is better than the introduction of impurities (homophase additives), since it does not distort the crystal lattice, does not alter the chemical composition of the substance and the nature of the distribution of electron density, and finally makes it possible to control readily and reversibly the concentration of conductivity electrons. The electric field can cause the dissociation of excitons with a large radius, as a result of which the exciton absorption bands are broadened. For example, Thomas and Hopfield[45] observed that the absorption lines corresponding to large-radius excitons in the spectrum of cadmium sulphide are broadened and merge in a field as low as 500 V cm^{-1}. Gross and Zakharchenya[46] observed a similar effect in copper(I) oxide, but in a field of 9 kV cm^{-1}. The difference in field strengths is consistent with the dimensions of the excitons: the exciton radius in copper(I) oxide is smaller by a factor of 2 than the radius of the analogous excitons (on the basis of the absorption spectrum) in cadmium sulphide and their bonding energy is higher by a factor of approximately 4. Consequently, the ionisation of excitons in copper(I) oxide requires an approximately 8 times higher field than in cadmium sulphide. The experimental data are qualitatively consistent with this rough estimate.

Kucherov et al.[47] and Lyashenko[48] established that the electrical conductivity of cadmium sulphide[47] and antimony sulphide[48] increases with time when an electric field is applied. This has been explained by the diffusion of the impurities and of the adsorbed gases in the direction of the field of which diminishes the concentration of the capture centres for free electrons and holes. Subsequently Cox and Tredgold[49] and also Kunin et al.[50] observed a change in the electrical conductivity and colour of $SrTiO_3$ single crystals in an electric field at an elevated temperature. During the first 1–2 min, the electrical conductivity diminished by an order of magnitude and then reached a value higher than at the beginning. It is suggested that the initial decrease of conductivity is caused by ionic polarisation and the subsequent increase is due to the increase of the concentration of V-type colour centres, formed under the influence of the electric field and altering the colour of the crystals. A sharp change in electrical conductivity during the application of the electric field (electric ageing) has been observed also for rutile single crystals[51] at 300°C, which has been attributed to the formation of new donor centres (defects) in the crystal lattice and a transition from p-type conductivity to n-type conductivity.

It has been established[52–54] that the potential barrier $\Delta\varphi$ (the difference between the electron work functions) of the metal–dielectric couple can be decreased with the aid of the electric field not only as a result of the Schottky effect but also owing to the penetration of the electrodes by the external electric field. Then, for low strengths E of the external electric field the condition $\Delta\varphi \propto \sqrt{E}$ holds and at high field strengths we have $\Delta\varphi \propto E$. The effect observed by the authors may predominate over the Schottky effect in high electric fields. It is useful to know this phenomenon in the study of the thermal decomposition of substances with a high-resistance additive in electric fields. The effect[55] observed in β-carotene and selenium is no less interesting. A transverse constant electric field superimposed on a longitudinal constant electric field causes periodic oscillations in solids at very low frequencies. The period of the observed current oscillations is influenced significantly by the strength of the transverse field, the intensity and length of the monochromatic light, the temperature of the specimen, and the composition of the atmosphere. The authors put forward two interesting hypotheses to account for the phenomenon.
1. In certain regions of semiconductors and probability of the localisation of charge carriers (electrons and holes) may increase with increase of the field strength and local unstable regions with a variable resistance may appear.
2. The cause of the observed current oscillations may be the formation of bulk-phase charges. The external field then disturbs locally the equilibrium current carrier density.

On the other hand, the application of a pulsed electric field and of illumination by flashes of ultraviolet light to a silver bromide photographic emulsion[56] induces physicochemical processes associated with the generation of a symmetry in the photoproducts and a decrease of the lifetime of the light-generated electrons. The intensity of these processes depends on the strength and duration of the application of the electric field.

In a strong electric field the long-wavelength limit of the intrinsic optical absorption of semiconductors (λ_g) must shift[57,58] towards longer wavelengths (the Franz–Keldysh effect). This can be explained by a definite probability of the migration of electrons from the valence band to the forbidden levels by a tunnel mechanism under the influence of the electric field. In other words, in a strong electric field the interaction of electrons with photons having a large

momentum can generate electron-hole pairs owing to the transition of some of the valence electrons to forbidden energy levels. In consequence of this process, electrons appear in the semiconductor above the valence band and their excitation to the conduction band requires a lower photon energy than for the electrons in the valence band. For this reason, a shift of λ_g towards lower energies is observed. By definition λ_g corresponds to the minimum energy of photons required for the excitation of electrons from the valence band to the conduction band of the crystal. The shift of λ_g for the semiconductor is observed also from absorption spectra and reflection spectra in constant and alternating fields. Seraphin and Bottka[59] proposed an analytical method for the interpretation of the electro-reflectance effect in semiconductors. The Franz–Keldysh theory has been extended to the majority of the field-induced changes in absorption and reflection spectra. The authors showed that the shift of λ_g in the field is not always towards longer wavelengths but only when the edge of the absorption (or reflection) band is parabolic. When the edge of the main band is saddle-shaped, the shift of λ_g is towards shorter light wavelengths. In degenerate semiconductors[60] (a high concentration of free charge carriers is characteristic of these) the electric field can shift λ_g much more owing to the "heating" of the charge carriers than at a concentration of carriers far from degeneracy. This additional shift of λ_g under the conditions of the field in degenerate semiconductors is called[61] the Burnstein shift. For example, in InSb for $n = 10^{19}$ cm^{-3} and 300 K the shift of λ_g is 0.50 eV via the Burnstein mechanism and 0.18 eV for a non-degenerate state.

The Franz-Keldysh effect has been frequently confirmed experimentally[62–66] for both atomic semiconductors (germanium and silicon) and for more complex substances with polar bonds: sulphides, selenides, tellurides, arsenides, and other typical semiconductors. For example, Moss[62] and Kireev et al.[63] measured the shift of the absorption edge in GaAs, CdS, and CdTe spectra by a 5 kV cm^{-1} electric field. The authors indicate a satisfactory agreement between the calculated and experimental shifts of λ_g. A difference was observed between the results for films and single crystals. There has been an interesting study by Dneprovskii et al.[64], who observed a shift of the absorption band in the spectra of mixed crystals of CdS_xCdSe_{1-x} semiconductors at liquid nitrogen temperature in electrostatic fields up to 30 kV cm^{-1}. The shift of λ_g for $CdS_{0.5}CdSe_{0.5}$ amounts to 30 Å in a somewhat weaker electric field than for $CdS_{0.7}CdSe_{0.3}$ crystals, which the authors attribute to a steeper absorption spectrum of the specimen. The most complete study of the shift of the intrinsic absorption band of a ZnTe single crystal in 60 kV cm^{-1} electric fields was that of Strel'tsov and Freidin[65]. The shift of λ_g is 0.004 eV. The effective mass of charge carriers $m^* = 0.16m_0$ was calculated from the shift, the result being in good agreement with the data obtained in other investigations. The shift of the absorption edge towards longer wavelengths leads to a change[66] of the absorption coefficient of PbI_2 single crystals in a 2.85×10^5 V cm^{-1} variable electric field, which is probably the result of the influence of the field on the transitions of excitons to the ground state.

One cannot rule out the possibility that the Franz–Keldysh effect also operates in non-classical semiconductors, which may be investigated in solid state chemistry. The determination[67,68] of the effective mass of free electrons and holes from the Franz–Keldysh effect is most important and promising: the energy of the shift of the long-wavelength absorption limit λ_g is inversely proportional to the reduced effective mass of charge carriers. It is also possible to obtain information about the structure of the valence levels and the levels of the conduction band involved in the electronic transitions. Knowing the effective mass of the majority charge carriers, it is possible to calculate[69,70] (using additional data for the thermo-e.m.f. and electrical conductivity) the concentration and mobility of the free charge carriers, which are needed to analyse the electronic processes in the thermal decomposition of solids. In a field of the order of 10^5 V cm^{-1} the minimum shift (in terms of energy) for semiconductors amounts to hundredths of an electron-volt[67], greatly exceeding the possible Stark effect[71], which also shifts λ_g. The method for the determination of the effective mass of charge carriers with the aid of the Franz–Keldysh effect is much simpler and no less accurate than the method of cyclotron resonance[72], which is the classical procedure.

While chemical bonds are redistributed by electronic processes, ionic processes are responsible for the transfer and redistribution of mass in the decomposition of solids. The ionic processes underlying[13,14] the formation and growth of the nuclei of the new phase are much slower than the electronic processes and for this reason they often constitute the rate-limiting stages in the thermal decomposition of solids. Naturally, the electric field, influencing the diffusion coefficient and mobility of ions, will influence also the thermal decomposition of solids. We shall analyse examples of this effect.

Geguzin and Solunskii[73] observed an effect of a constant 100 V cm^{-1} electric field on the kinetics of the development of diffusional porosity in alkali metal halide crystals at 650° C. It was suggested that the electric field, influencing the directed diffusion of charged vacancies, influences also the pore-formation process. Together with this phenomenon, the constant electric field can affect the phase composition of solid solutions. Thus Freimanis et al.[74] established that in ceramic specimens of barium niobate there exist two ferroelectric phases with orthorhombic and tetragonal symmetry. A 20–90 kV cm^{-1} electric field gives rise to phase transitions between the orthorhombic and tetragonal symmetry or conversely, depending on the orientation of the crystals. The magnitude of the effect depends on the field strength and the energy state of the specimens. The influence of the heat treatment of the specimens on electrical ageing has been studied by Harwood[75] for rutile. He established that the greatest changes in electrical conductivity occur when the field is applied along the *c* axis regardless of the direction in which the crystals are grown. It was suggested that the impairment of the dielectric properties of rutile as electrical ageing progresses is due to the drift of certain ions under the influence of the applied electric field. This experiment is important for the investigation of the anisotropy of the thermal decomposition of ionic crystals. The problem of the effect of the electric field on the alloying process is no less urgent in practice. Pavlienko et al.[76] observed that the rate of alloying of silicon by boron from the gas phase depends on the electric field, which causes an additional ionisation of boron at high temperatures in the gap between the electrodes and, when a positive potential is applied to the electrode, causes an accelerated diffusion of boron to silicon. The tracer atom technique makes it possible to investigate the rate of self-diffusion of various ions on the natural cleavage surfaces of single crystals in an electric field. Thus, it has been shown[77] that a field oriented along the surface of an NaCl single crystal can alter the rate of self-diffusion of sodium and chloride ions. On the other hand, a field oriented at right angles to the surface can influence the amount of the

"pumping away" of these ions, diffusing on the surface, into the bulk of the crystal.

The thermal decomposition of certain ionic salts, for example permanganates[78,79], is accompanied by intense cracking and atomisation of the crystals. The results of a study by Kononov et al.[80], who investigated the dust carried away from a fluidised bed furnace in the presence of an electric field in the working space of a reactor, are of interest for the investigation of the decomposition of such substances, with and without additives, in an electric field. The field reduced the amount of dust removed by a factor of 3–5 and caused the coagulation of dust particles whose size was between 40 and 80 μm.

The effect of the electric field on the physicochemical properties of silver bromide under illumination has been studied[81-83]. Although the aim was to investigate photolysis, the observation that the field influences ionic processes is useful also for the investigation of such processes in thermal decomposition. For example, Klein and Matejec[81] studied the formation and growth of silver nuclei on silver halide microcrystals (grains). When the silver halide grain is irradiated in a strong stationary field (of the order of 10 kV cm^{-1}) by ultraviolet light pulses lasting 10^{-2}–10^{-3} s, it is possible to accumulate photoelectrons on the anodic side and interstitial ions on the cathodic side, without the complete disappearance of these charge carriers in the remaining parts of the grain. As a result, better conditions are created on both the cathodic and anodic sides of the grain for the formation of nuclei compared with the rest of the grain. The formation of negative centres on pulsed illumination of a photographic emulsion based on silver bromide under the conditions of a pulsed electric field has been observed by Hamilton and Bready[82], who proposed a method for calculating the cationic conductivity. At room temperature the calculation yielded a conductivity differing only by an order of magnitude from the experimental value for silver bromide single crystals. The bulk-phase diffusion of cationic vacancies, arising in the photochemical decomposition, was also observed for the single crystals[83]. A semi-transparent metallic layer was deposited on the one side of the single crystal and a continuous silver layer, obtained by evaporation *in vacuo*, was deposited on the other side. The light intensity decreased by a factor e at a depth of 1.5 μm, but, owing to the electric field, a dark reaction took place on the other side of the single crystal, which resulted in a gradual increase of transparency of the silver layer and its final disappearance. This study was apparently the first in which the bulk-phase diffusion of cationic vacancies was observed experimentally. The problem of the diffusion of ions in an electric field is no less important. Thus, Arnikar and Chaure[84] studied the influence of γ-radiation and of the electric field on the diffusion of the tracer ions $^{45}Ca^{2+}$, $^{90}Sr^{2+}$, and $^{133}Ba^{2+}$ through calcite. The application of a 27–100 V cm^{-1} electric field increased the diffusion coefficients of all three ions in the direction of the field as well as in the opposite direction. This effect was explained by an increase in the probability of the diffusional jumps of the ions in the electric field. The authors' studies are of fundamental importance, since an increase of the rate of diffusion had not been observed previously in similar experiments[85,86] and an impression had been created that the electric field cannot influence the diffusion coefficients of ions.

All these observations are valuable and interesting for the development of a method for electrophysical studies on the thermal decomposition of solids in an electric field.

3. Influence of the Electric Field on Dislocations

The influence of dislocations on the rate of thermal decomposition of solids is well known[13,87,88]. The decomposition of solids usually begins from the surface at the point of emergence of dislocations and extends throughout the bulk of the substance. It is therefore necessary to know the influence of the external field on the behaviour of dislocations in solids. Sproull[89] investigated elastic deformation effects, arising as a result of the application of an electric field, in lithium fluoride crystals bent at 220°C. He established that the dislocations in lithium fluoride are charged and can migrate over distances which are not susceptible to measurement, and that a considerable proportion of the mechanical strain is electrostatic in nature. The migration of the dislocations caused by the electric field in lithium fluoride crystals reaches a maximum in the course of a fraction of a second. The excess of dislocations of the same sign in cubic NaCl type crystals can actually disturb the symmetry and can make the crystal anisotropic, which is extremely interesting for the investigation of the electrophysical properties and decomposition of crystals. The migration of dislocations under the influence of a steady electric field of up to 15 kV cm^{-1} leads to a decrease in the optical transmission by sodium chloride[90] at a wavelength of 220 nm. A strong electric field also intensifies the absorption of light in this optical region. The migration of charged dislocations in an 8 kV cm^{-1} electric field has been observed by following the migration of etching figures under the microscope in studies by Zagoruiko[91] and Shvidkovskii et al.[92] The minimum field in which the migration of dislocations was observed was found to have a strength of 2 kV cm^{-1}. It was suggested that the migration of dislocations is caused by electrostriction, by the direct action of electrical forces on the charged dislocation, or by the joint influence of both factors. Using a similar technique, Zuev and Turchinovich[93] studied the migration of dislocations in lithium fluoride crystals under the conditions of a constant electric field. The authors suggest that the electric field lowers the potential barrier to the thermal liberation of dislocations from fixation centres. The influence of the electric field on the structural changes in such solids has been studied by Trap and Stevels[94]. The authors observed in certain chalcogenide glasses a transition to two states with different electrical conductivities when the electric field was altered. The conductivities of these states can differ by many orders of magnitude (up to 7). The transition of the glasses from one state to the other took place in a period of about 10^{-6} s. Since the conductivities of solids are related solely to the concentration of charges and their mobility, it is easily understood that the electric field alters sharply in this case the conditions governing the occurrence of ionic and electronic processes.

4. Influence of the Electric Field on Luminescence

The initial stage in the thermal decomposition of solids may be accompanied by luminescence[38]. Despite the great possibilities which arise from the application of luminescence measurements, this method has not so far been used in the experimental techniques of solid state chemistry. We are not aware of any study of the thermal decomposition of solids employing the luminescence phenomenon. In investigations of the photolysis of solids there are examples of the use of luminescence measurement which are of interest also for the study of thermal decomposition. For example, Belous and Chibisov[95] used luminescence measurements to

study the photolysis of silver chloride. They established that, depending on their size, the silver nuclei can serve as traps for both electrons and holes. The hole traps are usually aggregates consisting of several atoms with pre-colloidal and colloidal degrees of dispersion. The thermal decomposition may be accompanied by luminescence in the following cases: 1. The thermal excitation of complex anions of self-activated[38,96] inorganic compounds, which usually contain transition metals with a partly filled 3*d* orbital. 2. The thermal decomposition of substances with homophase additives, which can serve as luminescence centres. 3. The thermal decomposition of substances in different gases, whose absorption may be accompanied by luminescence[97].

In view of the likely usefulness of luminescence measurements in the study of the mechanism of thermal decomposition, it is desirable to analyse the ways in which the electric field influences the luminescence process in solids. The electric field can be a source of a specific type of luminescence of solids — electroluminescence. Electroluminescence is observed when steady and alternating electric fields of several kV cm^{-1} are applied. The brightness of the glow then depends on the field strength, the field frequency, and the duration of application of the field. It is particularly characteristic of alternating electric fields. A few crystalline phosphors are capable of electroluminescence, but the mechanism of the generation of the glow has been by no means fully studied. Afanas'eva and Mikho[98] observed the electroluminescence of a microcrystalline alumina powder using a transparent electrode. The brightness of the luminescence is related exponentially to the exciting potential, which agrees well with the concept of an inhomogeneous distribution of the field in the specimen. The threshold potential for the occurrence of the electroluminescence of ZnCdS discs was reduced[99] when the specimens were irradiated with light in the spectral region corresponding to the excitation of the intrinsic or impurity photoconduction. In this way a relation was established between the electroluminescence and photoconductivity of the specimens. Electroluminescence was observed also in powdered tantalum pentoxide[100] on excitation by potential Π-pulses lasting 2×10^{-3}–3×10^{-2} s. The hypothesis of an inhomogeneous distribution of the electric field in the specimens made it possible to explain the shape of the curves describing the development of the luminescence. The electroluminescence of cadmium selenide single crystals, arising on excitation by variable 5–25 kV cm^{-1} electric fields, was studied by Ivanchenko[101]. The electric field caused appreciable heating of the crystals and the electroluminescence was observed at a high temperature. It was noted that the free electrons generated in the electric field and to some extent thermal electrons pass from the conduction zone to ionised acceptor levels. Assuming that the luminescence is excited by the electrons displaced by the field, Henich[102] and Curevich[103] proposed a mechanism of the electroluminescence of ZnS with an admixture of copper and chlorine. The holes formed in this process are localised at the luminescence centres and the electrons are displaced from the excitation region and are captured by traps.

Apart from initiating electroluminescence, the electric field can also influence[104–109] the intensity of other types of luminescence: thermoluminescence photoluminescence, and radioluminescence. For example, this has been established for Cu_2O, ZnS, and alkali metal halide crystals with additives. Thus Peka[104,105] observed an effect of constant electric fields up to 10^6 V cm^{-1} on the photoluminescence of copper(I) oxide. The magnitude of the effect depended on the treatment of the surface, the strength and sign of the electric field, the surrounding gas, and the wavelength of the light exciting the luminescence. The author explains this dependence by a change in the conditions governing the annihilation of excitons with the depth of screening on the Cu_2O surface. Busca et al.[106] determined the temperature variation of the effect of the electric field on the thermoluminescence of ZnS with copper additives. It is suggested that the electric field influences the capture of electrons by recombination centres, which consist of copper atoms, and this alters the intensity of the thermoluminescence. The influence of the electric field on the X-ray luminescence of phosphors based on KI–Tl at low excitation intensities is contradictory[107]. At the instant of application of the field the glow is quenched, but after a time it is intensified. This complex behaviour of the luminescence is difficult to interpret, although the most likely mechanism of the increase of the luminescence intensity is a reduction by the electric field of the radiationless recombinations outside the luminescence centres. The results obtained by Denks[108] for alkali metal iodides activated by thallium are close to those of Pologrudov and Penzina[107], but in this case the electric field resulted merely in an instantaneous decrease in the intensity of the thallium luminescence without a subsequent increase in intensity. The influence of the electric field on radioluminescence and thermoluminescence has been studied most completely by Volkov et al.[109] in alkali metal halide scintillators. Both positive and negative effects of electric fields up to 50 kV cm^{-1} were observed. Various experimental findings enabled the authors to conclude that the effect of the electric field on radioluminescence and thermoluminescence reduces to a redistribution of the probabilities of radiative and radiationless processes. It follows from the studies quoted above that the most likely mechanism of the influence of the electric field on the intensity of the luminescence of solids is a shift of the cloud of quasifree electrons in the electric field, which reduces their concentration in the glowing region of the crystalline phosphor and diminishes the number of radiative recombinations. The influence of the electric field on luminescence can be used to study the recombination of electrons on the surface of crystals.

The possibility that an electric field quenches the photoluminescence, thermoluminescence, and radioluminescence of zinc sulphide with admixtures of copper and chlorine and also of alkali metal halide crystals has been studied[110–115]. Thus Vereshchagin et al.[110] observed the quenching of the luminescence of ZnS powder with an admixture of copper in constant and pulsed fields of the same polarity. The variable electric field led to a brief change in the brightness of the photoluminescence. Several possible mechanisms have been proposed for the quenching of photoluminescence: (1) in the region of electroluminescence the electric field accelerates free electrons: (2) weak electric fields cause the migration of holes, liberated from the emission centres by heat or light, to quenching centres; (3) strong electric fields ionise the luminescence centres.

The quenching by the electric field of the photoluminescence of a powdered ZnS phosphor with an admixture of chlorine[111] occurs differently with light corresponding to different spectral bands. It is suggested that the luminescence bands are caused by various luminescence centres differing from one another in their energy structure. The mechanism of the quenching of the photoluminescence is believed to involve the thermoelectric saturation of the luminescence centres by electrons ionised on photoexcitation. However, a similar mechanism can lead to an increased intensity of the photoluminescence due to the electric field when the electronic levels of the activator in the crystalline phosphor are above the middle of the forbidden gap. Andrianov and

Bogacheva[112] reviewed studies on the effect of the electric field on the thermoluminescence of activated zinc sulphide and noted three possible mechanisms for the quenching of the luminescence: (1) the field accelerates free electrons and holes; (2) the field displaces the charges to sites of radiationless transitions; (3) the field alters the potential barrier to the thermal liberation of the electrons and holes localised after excitation.

Denks et al.[113] and Grigor'ev et al.[114] applied the mechanism of the quenching of the ZnS luminescence in an electric field to alkali metal halide scintillators with an admixture of thallium, where a 10^5 V cm^{-1} electric field weakened the photoscintillation by 25%. The quenching of the luminescence of alkali metal halide crystalline phosphors by the electric field is of a general type and the authors believe it to be related to the separating effect of the field, which prevents the recombination of electrons and holes. An example of the quenching of the thermoluminescence of alkali metal halide crystals doped with thallium and indium by a 50 kV cm^{-1} electric field is provided by the study of Grigor'ev et al.[115] The field intensified the thermoluminescence after prolonged application and quenched it after brief application. The observed intensification of the thermoluminescence was attributed by the authors to the decrease in the potential barrier to the autolocalised holes.

5. Phase Transition in the Electric Field

Phase transitions are usually accompanied[116,117] by anomalies in the temperature dependence of the rate of decomposition and conductivity under the conditions for investigating the mechanism of the thermal decomposition of the material. To develop electrophysical methods[1] for the investigation of the thermal decomposition of solids, it is necessary to know how the electric field affects their phase transitions.

A semiconductor–metal phase transition has been observed in a number of transition metal oxides, such as vanadium oxides, and has been explained by the instability of the electronic excitation system[118–120]. Owing to the intense electron-phonon interaction, the crystal lattice of the oxide is then rearranged. Andreev et al.[121] observed a sharp jump in the conductivity of V_2O_5 (an increase by 5 orders of magnitude) in a 10^4 V cm^{-1} field, which indicated the appearance of metallic conduction. The electric field shifts the temperature of the phase transition. The thermal effect and the Poole effect do not then play a significant role. It has been suggested that the increase of conductivity is caused by the decrease of the width of the forbidden gap due to the piezoelectric effect, which is the main cause of the semiconductor–metal phase transition. Valiev et al.[122] observed a similar phase transition under the influence of the electric field in another crystalline vanadium oxide (VO_2) at $T < T_c$ (T_c is the temperature of the VO_2 phase transition). The authors attribute the phase transition to a change in the lattice parameters in the electric field (the reverse piezoelectric effect). The influence of the electric field on the ferroelectric phase transition in barium metatitanate has been studied[123] and a change in the phase transition temperature in the electric field has been demonstrated. The same problem was investigated by Zarembskaya et al.[124] in a study of the influence of a constant electric field on the temperature of the phase transition in triglycine fluoroberyllate. The ferroelectric phase transition was recorded on the basis of a maximum in the dielectric constant measured at a frequency of 1 kHz in the temperature range 40–90°C. The application of the electric field decreased the dielectric constant of triglycine fluoroberyllate and shifted the ferroelectric phase transition to higher temperatures.

6. Adsorption in the Electric Field

The thermal decomposition of solids is frequently carried out in different vapours and gases: for example, in water vapour[125,126], in ammonia vapour[127], in oxygen[128], and in carbon dioxide[129]. Such studies are performed either to establish an effect of different components of the atmosphere on the decompositon kinetics, or to investigate the autocatalytic influence of the gaseous decomposition products of the initial substance, or to investigate the electronic stages of the decomposition process. In view of this and also bearing in mind the development of electrophysical methods[1] for the investigation of the thermal decomposition of solids, it is necessary to formulate clearly the specific influence of the electric field on the adsorption of gases.

The Fermi level can be regarded[130] as the regulator of the chemisorption properties of the semiconductor surface. The position of the Fermi level fixes the concentration of the electron and hole gas on the semiconductor surface. The surface and bulk phase of the semiconductor have a common Fermi level at equilibrium. The chemisorption of gases entails the charging[130,131] of the semiconductor surface, which causes the bending of the energy bands at the surface. This alters the position of the Fermi level in the energy spectrum of the crystal on the surface compared with the bulk phase. Factors which shift the Fermi level in the bulk of the crystal (which corresponds to a change in conductivity) shift it also on the surface, altering the catalytic activity of the semiconductor. However, under certain conditions[130] the position of the Fermi level on the crystal surface is independent of its position in the bulk phase (the case of a quasi-isolated surface).

Vol'kenshtein and coworkers[130,132–134] predicted theoretically the possible changes in the electronic properties of the surfaces of semiconductors under the influence of the electric field. If a semiconductor plate is placed between the plates of a planar air condenser, then a positive charge will be induced on one side of the semiconductor and a negative charge on the other. The semiconductor as a whole remains electrically neutral, but the adsorption capacity of its sides is altered. Vol'kenshtein's theoretical predictions have been frequently confirmed experimentally. For example, Stadnik and coworkers[135–140] demonstrated the influence of a constant electric field on the rate of liberation of various products of heterogeneous catalytic reactions, one of the stages of which is adsorption. For instance, studies have been made on the oxidation of the propane–butane mixture in the presence of platinum with formation of peroxides, aldehydes, and acids, the oxidation of methanol to formaldehyde on zinc oxide and a zinc oxide (60%)–copper(II) oxide (40%) mixture, the oxidation of various alcohols on silver, and the oxidation of sulphur dioxide to the trioxide on a platinum catalyst. The field can influence only the electronic stages of heterogeneous catalytic reactions and therefore its influence on the rate of reaction leads to the converse conclusion that electronic processes take place and play a significant role in the given heterogenous process. In the examples quoted the catalysts are metals. This does not contradict the previous conclusions reached for semiconductors, since the catalytic activity of metals is due to the presence of a very thin layer of oxides, which are semiconductors[130,141].

The gas–solid interaction, which frequently accompanies thermal decomposition, gives rise to the adsorption phenomenon. The adsorption of gases alters[142] various electrophysical parameters of the surface of solids, primarily their conductivity. A decrease of the concentration of charge carriers as a result of chemisorption at the points of contact between the particles in "sintered" specimens can give rise[131] to "blocking" layers due to the migration of the gas along the pores. These layers cause a particularly marked change in the conductivity of semiconductors. The adsorbed gas species can themselves behave as electron donors and acceptors if they react with the solid. The activation energy for chemisorption on semiconductors is in most cases considerable. The adsorbed gas molecules charge the semiconductor surface[130] and a potential difference, the value of which can be very high, is established between the surface and the bulk phase. For example, in the chemisorption of oxygen on zinc oxide[131] a 10^6 V cm^{-1} field is established between the surface and the bulk phase. The impurity ions can diffuse into the bulk phase under the influence of the electric field. The surface potential can be altered by the field effect and adsorption methods. Under certain conditions, both effects can operate simultaneously. Thus in very high fields and in measurements in a high vacuum the adsorption—desorption equilibrium can be displaced by the electric field, i.e. electroadsorption and electrodesorption is possible. In measurements in a vacuum of the order of 10^{-5}–10^{-6} torr, for a field strength less than 10^6 V cm^{-1}, the electroadsorption effect does not influence the field effect[142]. Unfortunately the electrodesorption effect has so far been studied only on classical semiconductors.

Flitner[143] investigated the effect of the field on germanium under the condition of the adsorption of oxygen, ozone, and water vapour. He established that ozone increases the number of fast states. Slow energy states arise on the surface of germanium in the adsorption of oxygen. A moist atmosphere influences the fast states, but does not alter the charge of the slow states. The author believes that this indicates the formation of germanium oxide on the germanium surface. Lyashenko and coworkers[144,145] observed the influence of the electric field on the desorption of gases from a germanium film. The resistance of the film increased following the desorption of gases. It is interesting that an increase of gas pressure in the system was observed only after the first application of the electric field. When the desorbed gas is evacuated, a repeated application of the field within the same limits does not alter the gas pressure. However, after the readsorption of the gas the electrodesorption process is again observed. The change of pressure in the system and of the resistance of germanium are due to the same cause—the change in the surface charge of the semiconductor. The gas contained hydrogen, hydrocarbons (oil from the pump), nitrogen, and nitric oxide. Mainly nitrogen was electrodesorbed. In the case of a negative potential on germanium this phenomenon was not observed. The external field reduced the negative charge on the surface of germanium, which led to the desorption of the gas. The electrodesorption effect was not observed on germanium films with a thickness greater than the screening radius. The studies by Mikheeva and Keier[146–148], who investigated the influence of a constant transverse electric field on the chemisorption properties of *n*-type germanium in relation to methanol and oxygen, constitute a logical continuation of studies on the adsorption capacity of germanium in the electric field. The field, leading to an increase in the surface potential, which is positive on germanium, and to an upward bending of the bands), resulted in the appearance of charged chemisorbed methanol species. In the absence of the field under these conditions (at 27°C and a pressure of 10^{-2} torr) methanol was not adsorbed. It was established that a transverse electric field disturbs the electronic equilibrium between the surface and bulk-phase bands. After the application of this field, the equilibrium between the surface and the bulk phase was restored in 1.5 to 2.0 h. When a field is applied, there is a possibility of side effects associated with the ionisation, polarisation, and orientation of the molecules in the gas phase. Therefore measurements must be made at a pressure of the order of 10^{-2}–10^{-3} torr. It was also established that the change in the adsorption properties of germanium in the electric field is caused by the change in the position of the Fermi level and the filling of the surface energy levels with electrons. The influence of the field on the adsorption of oxygen was observed only following the application of a negative potential to germanium, which decreases the electron work function. By measuring the relaxation of the conductivity of germanium when the field was switched on and off *in vacuo* and in an atmosphere of oxygen, it was shown that oxygen does not form new acceptor centres and that adsorption takes place on the existing surface acceptor centres. It was suggested that the active adsorption centres on germanium are slow donor states for methanol and slow acceptor states for the adsorption of oxygen. It was concluded that the adsorption properties of semiconductors are determined by the chemical state of the surface and the presence of active adsorption centres. Similar studies on the effect of a steady electric field on the adsorption of CO_2 were carried out by Ivankiv and coworkers[149,150] using thin tellurium films. Electrodes (silver, aquadag) for the measurement of the resistance were located along the edges of the film and a field electrode was placed on the other side of the support. Simultaneously measurements were made of the CO_2 pressure, and of the film resistance. The experiment on the electrodesorption of CO_2 from the tellurium film was performed in a vacuum of 5×10^{-9} torr in a 10^5 V cm^{-1} field. Under these conditions, with a positive potential on the semiconductor, CO_2 was electrodesorbed. At a negative potential a slight adsorption of CO_2 was observed on the film. The same workers[151,152] investigated the adsorption of oxygen and water vapour in an electric field on epitaxial β-HgS films with *n*-type conductivity. The adsorption was investigated on the basis of the changes in film conductivity. The application of a positive potential to the film increased the degree of adsorption of donor molecule and decreased the degree of adsorption of acceptor molecules, while at a negative potential the opposite effect was observed. The removal of the field restored the conductivity of the previous value owing to intense chemisorption on certain sections of the film. It was concluded that the chemisorption of oxygen on mercury sulphide is enhanced following the application of the electric field.

The conductivity of potassium permanganate single crystals has been investigated in water and ethanol vapours[153]. Single crystals, clamped between graphite electrodes, were alternately placed in desiccators [sic] containing water or alcohol and in a desiccator with phosphorus pentoxide. A 100 V cm^{-1} electrostatic field acted constantly or was applied periodically (at the instant of measurement of the conductivity). As potassium permanganate was made moist under the conditions of a briefly applied field, its conductivity steadily increased, tending to saturation. On the other hand in a steady field the conductivity passed through a maximum after the first moistening process. Due to the repeated drying and treatment of the crystals in water

and ethanol vapours, residual effects appeared in the changes of the conductivity of the single crystals, which were accounted for by the influence of the field on the chemisorption of the polar vapours.

7. The Change in the Properties of the Surfaces of Solids under the Influence of the Electric Field.

Since the thermal decomposition of solids begins as a rule from the surface[13,14], the state of the surface plays a major role in the development of the decomposition process. There is usually a complete system of discrete and continuously distributed energy levels on the surface of crystals[142,154–159], which may have different origins. These may be Tamm levels, arising on the surface as the result of the termination of the crystal lattice, and also energy levels associated with impurities or due to surface defects in the crystal lattice. Finally surface levels may be associated with the adsorption of molecules from the surrounding gas. The local energy levels on the surface and the associated surface charge lead to the bending of the energy bands near the surface, which is reflected in a significant change of the electron field work function and photoelectric and other properties. Often the state of the surface largely determines the course of the physical processes associated with the bulk phase of the crystal. Thus the surface levels can behave as recombination centres and can influence the lifetime of the non-equilibrium charge carriers in the specimen. Owing to the presence of the potential "well" near the semiconductor surface, the migration of the charge carriers in the surface region differs significantly from their migration in the bulk phase. This leads to a change in the mobility of the carriers owing to the additional scattering of the electrons and holes on the surfaces. The change in the energy state of the surface is attributed to a change in a particular surface parameter of the substance—the surface potential φ_S. This quantity can be determined as the difference between the potential energy of the electrons in the bulk phase and on the surface of the crystal. There are many experimental methods for the measurement of the surface potential, the most convenient of which is the field effect method.

The field effect is characteristic of semiconducting substances and consists in a change of the conductivity of the semiconductor following the application of a potential difference at right angles to its surface (and to the direction of the current). The field effect was first observed on copper(I) oxide by Schockley and Pearson[154]. It can be interpreted as follows. If one assembles a condenser one plate of which consists of the specimen and the other of a metal, using an intervening layer of an insulator with a high dielectric constant, and an electric field is applied to the condenser, then a space charge is created near the semiconductor surface, neutralising the charge on the metallic plate. Thus Lashkarev and Lyashenko[155] continued the study of the field effect on copper(I) oxide and defined rigorously the semiconductor surface as a layer with a thickness equal to the free path of the charge carriers. The surface charge constitutes an obstacle to the imposition of an external electric field on the semiconductor. If a negative potential is applied to the metallic plate of the condenser, the semiconductor plate becomes positively charged. This charge is localised in the bulk phase and on the surface of the semiconductor and the neutrality of the latter is disturbed, the energy bands being bent upwards relative to the Fermi level. The decrease of the degree of filling of the surface level by electrons (which corresponds to an upward bending of the bands) leads to the appearance of an additional surface charge, i.e. to the screening of the external field. As a result of the field effect, the electron work function of thin layers of copper(I) oxide is greater than that of thick layers by 0.13–0.15 eV. Thus a considerable proportion of the charge induced by the electric field is captured[142,155–157] by the surface states and the bulk phase of the semiconductor is electrically neutral. If the metallic plate is positively charged, a negative charge is induced on the surface of the semiconductor and the surface region of the bulk phase of the conductor is positively charged. The thickness of the layer screening the external charge in the semiconductor is inversely proportional to the square root of the equilibrium concentration of its charge carriers outside the limits of the space charge. The bulk-phase charge carriers near the surface contribute to the conductivity of the specimen, in contrast to the stationary carriers in the surface energy levels[158]. By measuring the resistance of the specimen along the surface layer for different electric field strengths, it is possible to determine the change in conductivity associated with the applied field. To increase the accuracy of the measurements, the specimen should be made fairly thin, so that the change in the surface resistance constitutes an appreciable proportion of the total resistance of the specimen. The field effect can be investigated[158] in steady and alternating fields at frequencies up to 10^8 Hz. In an alternating field the degree of screening of the surface from the bulk phase is reduced at higher frequencies, and it becomes constant from 10^3 Hz up to 10^7 Hz. The thickness of the charged region near the surface of semiconductors is usually[159] of the order of 10^{-4}–10^{-6} cm and the mobility of the charge carriers in this layer depends on the thickness of the semiconductor. When the field effect method is used to measure the surface potential, the density of the surface states does not change, in contrast to the absorption method. When a transverse electric field is switched on, an induced charge is initially created at the surface and then equilibrium is established between the conduction band, the valence band, and the fast surface states with a time constant of 10^{-7}–10^{-4} s, as a result of diffusion, capture, and recombination. After this, an equilibrium degree of filling of slow surface states is established during a period from several seconds to 1 h. Ultimately the concentration of surface levels remains unchanged during the measurements and only the degree of their filling is altered. A continuous variation of the surface potential within fairly wide limits up to the minimum in the surface conductivity of the crystal can be readily achieved by the field effect method.

The type of surface conductivity and the relation between the degree of bending of the bands and the applied potential can be determined, the charge in the region near the surface can be discovered, and the mechanism of the surface recombination of charge carriers can be investigated by measuring the field effect under steady-state conditions[142,160–166]. Finally the field effect method makes it possible to determine whether or not the energy spectrum of the surface levels is continuous or discrete and their concentrations and energy positions can be determined. The study of the kinetics of the field effect (non-steady-state case) makes it possible to calculate the relaxation time of the surface levels and to elucidate the mechanism of the exchange of charge carriers between the bands in the bulk phase and the surface energy levels. A theory of the field effect has been devised for band semiconductors, but, as shown by Sandomirskii and Pyasta[160], it is applicable also to

polaron semiconductors with jump conductivity. In particular potassium permanganate, a classical system in solid state chemistry, is a polaron semiconductor[37]. The field effect has been observed[166] also in organic semiconductors. Thus Petrova and Rozenshtein[166] observed the field effect in a number of organic semiconductor films obtained by vacuum sublimation. The authors determined the sign of the conductivity of the test substances and observed the enrichment and depletion of the specimens in charge carriers under the influence of the electric field. It was concluded that slow states are characteristic of organic semiconductors. Consequently the type of chemical bond in solids does not play a decisive role in the manifestation of the field effect.

Measurement of the field effect using an alternating current yields information about the time characteristics of the surface traps, which measurements with a direct current fail to do. Whereas the field effects measured using a direct current are frequently masked by slow states, with an alternating current they are clearly manifested. Mathematical treatment of the frequency characteristics of the field effect yields quantitative data on the distribution of surface states with different time constants. Frolov et al.[167], who studied the influence of the thickness of silicon oxide on the field effect in silicon, observed a correlation between the thickness of the surface oxide layer and the concentration of surface electronic states in etched silicon specimens. It was shown that the nature of the fast surface states is determined by the structural defects at the semiconductor–oxide boundary. By studying the relation between the surface conductivity of silicon and the strength of a variable transverse field, Einspruch[168] showed that, under the experimental conditions, most of the charge induced by the field is captures by surface layers. Esaki et al.[169] studied the influence of the field effect on the conductivity of the contact layer in germanium–gallium arsenide heterojunctions. The mobilities found in the contact layer proved to be constant for fields in the range 2×10^4–5×10^5 V cm^{-1}. This case permits a simple investigation of the surface conductivity of semiconductors. The field effect in a high-resistance zinc oxide powder mixed with a silicone resin[170] showed that its magnitude and time constant in such specimens depend more on the associated charges than on the free charges, in contrast to low-resistance semiconductors. The rate of recombination of free electrons and the concentration of electron traps were calculated from the change in photoconductivity as a function of the transverse electric field.

Using the classical method[171] for the investigation of the field effect on zinc oxide single crystals, it was established that the surface potential of zinc oxide is negative and the specific conductance of the specimen increases rapidly with increase of the applied potential. It has been suggested that there are acceptor oxygen levels on the surface of zinc oxide to which electrons are withdrawn from the region of the bulk phase near the surface under the influence of the field. As a result, the layer of the bulk phase near the surface is depleted in electrons and their concentration on the surface increases. At a high concentration the acceptor levels on the surface of the ZnO crystals may be split off[172] as a band, which leads to an increase in the surface conductivity with increasing electric field strength. The bulk-phase specific conductance of the specimen then diminishes. For anisotropic semiconductor crystals[173], the relation between the transverse and longitudinal alternating currents is linear. This makes it possible to control the current in anisotropic semiconductors.

A steady influence of a constant electric field on surfaces has been established in a number of studies.[174–176] Thus Costa and Murphy[174] observed a persistent internal polarisation of a sulphur single crystal due to the operation of the electric field, the removal of which requires the application of external energy. It was established that the relation between this energy and the decrease of the polarisation is exponential. In amorphous selenium the phenomenon of residual polarisation, which decays exponentially as a function of time, was observed by Nasledov and Malyshev[175]. The mechanism of this phenomenon has not so far been elucidated, although it has been stated that the electrons get "stuck" within or on the surface of selenium. CdS single crystals placed between the plates of a charged condenser are quasineutral[176]. However, owing to the inhomogeneous bulk-phase conductivity of CdS, the charges are polarised and the polarisation may persist for a long time. It is suggested that in a strong electric field there is an injection of electrons at the cathode and not a limitation of the space charge.

The problem of the preparation of specimens for thermal decomposition is no less urgent. Ziman[177] reviewed studies on methods for the elimination of solid impurity particles from surfaces by the application of a high steady electric field. The initial specimen is earthed and exposed to the field via an air gap. The material of the field electrode does not affect the degree of purification of the dust-covered surface of solids. It is suggested that the dust particles are removed as a result of their becoming charged in the electric field. An electrical interaction then arises between the particles and the electrode, which tends to abstract the particles from the support.

In studies on the electrophysical properties of semiconductors and dielectrics attempts are made to carry out measurements in the region where Ohm's law holds. This is done to eliminate side effects: contact resistances and the Poole effect. However, it is not always possible to avoid the side effects and it is necessary to formulate clearly the influence of the field on these effects. The Poole effect[178,179] can be observed only for high-resistance substances in fields of 10^3–10^4 V cm^{-1}. The electrical breakdown of a layer of dielectric thicker than 10^{-5} cm occurs in fields of $(1–5) \times 10^6$ V cm^{-1}, which increase with decrease of the thickness. As the field increases, there is a rise in the concentration of charge carriers and not an increase of mobility[179]. Injection of charge carriers from the electrodes is one of the causes of the Poole effect, consisting in a rapid increase of the current with potential, which follows from Ohm's law. The knowledge of the relation between the field effect and the properties of the point contact is no less important in experimental studies. Nesmelova[180] stated that near the point contact the electric field has both normal and tangential components in relation to the surface. The presence of the normal component leads to the bending of the energy bands, similarly to the field effect, and hence to a change in the conductivity of the specimen. Then the dependence of the conductivity of the specimen on the applied potential should be minimal. Guerci and coworkers[181,182] observed the influence of a steady transverse electric field on the lag of the photocurrent in CdS crystals behind the instant when light is switched on. This lag was proportional to the electric field applied at right angles. They suggested that the transverse field disturbed the ohmicity of the contact and consequently reduced the current through a cadmium sulphide crystal. The same field induced oscillations in the photocurrent within the specimen, which made it possible to separate the surface and bulk-phase components of the photoconductivity.

Thus the study of the field effect yields important information about the electronic processes on the surfaces of solids, which can be used to understand the influence of the field on the development of the decomposition process.

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The examples analysed leave no doubt about the great but hitherto incompletely utilised scope of the electric field as the foundation of a method for the investigation of the mechanism of thermal decomposition and as a procedure for stimulating the thermal decomposition of solids. Electrophysical studies of the thermal decomposition of solids constitute an effective means of comprehending the essential physical nature of the elementary stages in the decomposition reactions and the mechanisms of the electronic and ionic processes whereby the initial substance is converted into the reaction products. These problems constitute the corner stone of solid state chemistry.

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Alkylation and Arylation of Unsaturated Compounds with the Aid of Transition Metal Complexes

L.G.Volkova, I.Ya.Levitin, and M.E.Vol'pin

Methods for the alkylation and arylation of unsaturated compounds with the aid of Group VIII metal complexes are examined and both the preparative aspects and the mechanism of the reactions involving the introduction of various organic groups into olefins are discussed.
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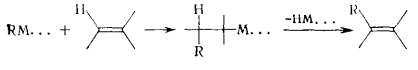
I. INTRODUCTION

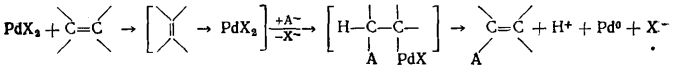
In the chemistry of olefins reactions occurring under the influence of transition metal compounds have been acquiring increasing importance. Important industrial processes such as polymerisation of olefins at low temperatures and pressures, direct oxidation of propene to acrolein, the oxidation of propene and ammonia to acrylonitrile, the oxidation of olefins in the presence of vanadium salts with formation of carbonyl compounds and vinyl esters of carboxylic acids, and the hydroformylation and disproportionation of olefins were introduced in the course of the last two decades.

Significant advances have also been achieved in the development of methods for the consecutive growth of the carbon chain in unsaturated compounds. The classical Meerwein reaction[1]—the arylation of olefins by diazonium salts in the presence of copper compounds—is of limited importance, since it makes it possible to introduce only an aromatic residue into the unsaturated molecule. The use of Group VIII metal complexes has given rise to good prospects for the introduction of organic groups into olefins. Their application is based on the capacity of certain organometallic σ derivatives of these elements, particularly those of palladium, to add to the double bond and on the instability of the addition products with respect to β-elimination:



Although the oligomerisation, disproportionation, and hydroformylation of olefins should be formally included in the type of processes under consideration, we shall not discuss them here, since an extensive literature has been devoted to each of these reactions. The oligomerisation and cyclooligomerisation reactions[2] are particularly characteristic of compounds with the C≡C triple bond in the presence of Group VIII metal complexes, while the growth of the carbon chain in acetylene derivatives is achieved more readily by the methods which have been thoroughly developed in organic chemistry. For this reason, attention will be concentrated in the present review on the introduction of alkyl and aryl groups into compounds with a C=C double bond, which is of preparative interest.

The interaction of olefins with transition metal complexes is known to involve in many instances the ready formation of π complexes. As a result of the changes in the electronic structure of the unsaturated ligand, the reactivity of the double bond in many π complexes in relation to nucleophilic reagents increases compared with the free olefin. Nucleophilic addition to π complexes has been comparatively thoroughly investigated in the chemistry of palladium. If there are no factors favouring the stabilisation of metal–carbon σ bond in the resulting compound (for example the influence of other ligands or of chelate formation), the hydride is eliminated and the overall process reduces to the substitution of the vinyl hydrogen:

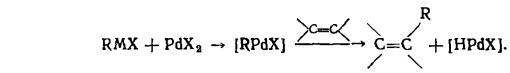


The mechanism of such reactions has been thoroughly studied by Moiseev in the oxidation of olefins by palladium(II) compounds[3]. It was shown that the intermediates in this reaction are labile organopalladium σ compounds obtained as a result of a rearrangement of the palladium complex containing the olefin, joined by a π bond, and a solvent molecule[4-6]. These fundamental stages are apparently characteristic of the majority of the reactions discussed in the present review.

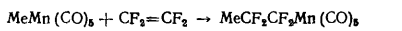
II. ALKYLATION AND ARYLATION OF OLEFINS BY ORGANIC TRANSITION METAL σ DERIVATIVES OBTAINED BY DOUBLE DECOMPOSITION REACTIONS BETWEEN GROUP VIII METAL SALTS AND ORGANOMETALLIC COMPOUNDS

The possibility, in principle, of the formation of labile organopalladium σ complexes in double decomposition reactions of organomercury compounds with palladium salts was demonstrated by Moiseev in 1960[4]. Ways of employing such complexes in organic syntheses were discovered in 1968 by Heck[7]. He succeeded in synthesising a wide range of alkylated and arylated olefins by

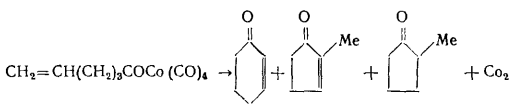
allowing the olefin to react jointly with a transition metal salt and an organic derivative of a non-transition metal[7-12]:



It is noteworthy that, even before these investigations by Heck, instances were known where the interaction of alkyl σ complexes of transition metals with olefins resulted in the formation of a new carbon–carbon bond, namely the addition of methylmanganese pentacarbonyl to tetrafluoroethylene with formation of a new organometallic complex[13]:



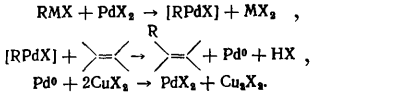
and the cyclisation of the organic ligand of hex-5-enoylcobalt tetracarbonyl, which resulted in a mixture of cyclohexenone, 2-methylcyclopentenone, and 2-methylcyclopentanone[14]:



A characteristic feature of the new stage in the wide-scale application of transition metal compounds for the alkylation and arylation of olefins was the use of stable organometallic compounds of non-transition metals as the source of organic groups. Heck and other investigators showed[7,15-20] that such donors or organic groups may be derivatives of lithium, magnesium, thallium, mercury, tin, and lead. However, these organometallic compounds are either sensitive to air and moisture (organolithium and organomagnesium compounds) or are highly toxic (organic derivatives of mercury, tin, thallium, and lead), so that their use in many cases involves significant difficulties. The recently discovered possibility of using organosilicon compounds—alkyl- and aryl-silanes, which are stable, non-toxic, and relatively readily available—as sources of alkyl and aryl groups in these reactions[21,22] is therefore of interest. Symmetrical organic derivatives Ar_2E, where E = P, As, Sb, or Bi, can also be used for arylation[23,24]. It has been shown that stable alkyl and aryl σ complexes of cobalt, rhodium, and iron with chelating ligands RM(Chel), where R = Me, Ph, or $PhCH_2$ and Chel = bis(dimethylglyoximate), bis(salicylidenato)ethylenediamine, and corrin and phthalocyanine ligands[25,27].

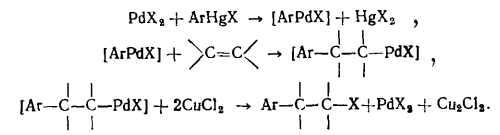
In most cases the above reactions occur at room temperature in various polar solvents, such as methanol, acetonitrile, acetic acid, and tetrahydrofuran and lead to the formation of substituted olefins in yields which are nearly quantitative in many cases. In arylation with the aid of compounds of Group VA elements more severe conditions are required (refluxing in an acetic acid–dioxan mixture)[24], probably in order to suppress the coordination of palladium to these compounds via a heteroatom.

The most active "transferring" agents for organic groups in these reactions are palladium compounds, the rhodium, ruthenium, and nickel complexes being less active[7]. Upon reaction, the transition metals acquire the zero oxidation state. The use of suitable reoxidising agents, such as copper(II) chloride, and iron and mercury salts, permits their regeneration and thus makes the reaction catalytic[7]:



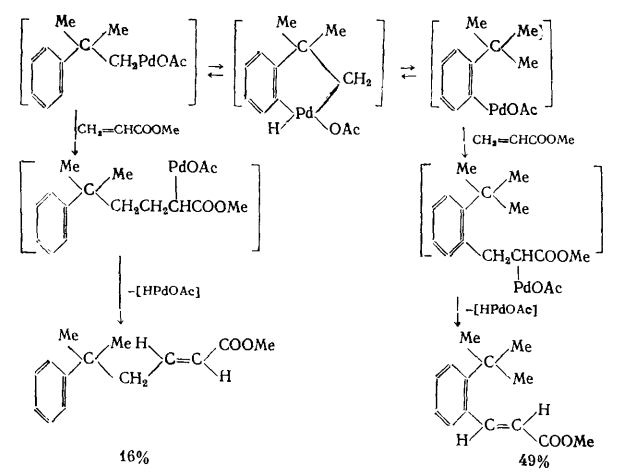
Copper(II) chloride can be regenerated from copper(I) chloride with the aid of atmospheric oxygen and hydrogen chloride.

In those cases where the concentration of the copper salt in solution exceeds 0.5 M halogeno-derivatives are also formed and the halogenoethylation reaction can become the main one[10]. For example, the reaction of phenylmercury chloride with ethylene in the presence of catalytic amounts of $PdCl_2$ and $CuCl_2$ at a concentration of 2 M results in the formation of phenylethyl chloride in 76% yield:

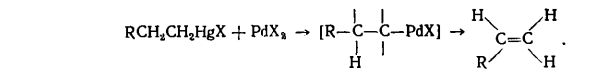


This reaction is itself also very useful for synthetic organic chemistry, because there is no other way of adding, in a single stage, a 2-halogenoethyl group to an olefin.

Alkylation of unsaturated compounds by organopalladium σ complexes makes it possible to introduce into olefins alkyl groups without a β-hydrogen atom, such as the methyl, carboxyalkyl[7], benzyl, and neopentyl[28] groups. From the standpoint of synthesis, the transfer of the neopentyl group as a method for the introduction of a quaternary carbon atom into an unsaturated molecule is of special interest. The transfer of another group fully substituted in the β-position—2-methyl-2-phenylpropyl—is accompanied by an interesting rearrangement, probably in the stage involving the formation of the organopalladium σ compound, so that the normal product is accompanied by an olefin with the *o*-(t-butyl)-phenyl substituent at the double bond:

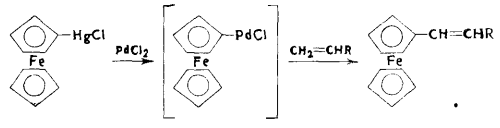


The attempts to transfer groups containing hydrogen in the β-position were unsuccessful: the olefin corresponding to β-elimination from the alkyl group was obtained instead of the alkylated products[7]:



Like alkyl groups without β-hydrogen, aryl groups with various substituents can be introduced into unsaturated molecules with the aid of transition metals[7]. Under these conditions, powerful electron-donating groups such as the methoxy-, hydroxy-, and diethylamino-groups in the *ortho*- and *para*-positions, lower the yield of the arylated olefins; substituents with a marked capacity for coordination to metals, for example the amino-group, hinder still more the reaction or preclude it altogether.

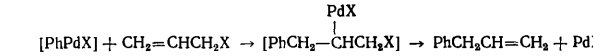
Subsequently arylation by a non-benzenoid aromatic system was achieved—the ferrocenyl residue was introduced into olefins[29]:



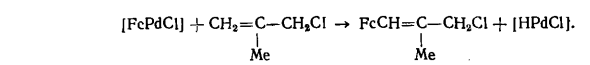
The nature of the olefin also plays a significant role in the above reaction. In particular the arylation of olefins with the normal structure and a short chain proceeds more readily and with higher yields. The relative rates of arylation decrease in the following sequence[7]:

$$\underset{14\,000}{CH_2{=}CH_2} > \underset{970}{CH_2{=}CHCOOMe} > \underset{220}{MeCH{=}CH_2} > \underset{42}{PhCH{=}CH_2} > \underset{1}{MeCPh{=}CH_2}.$$

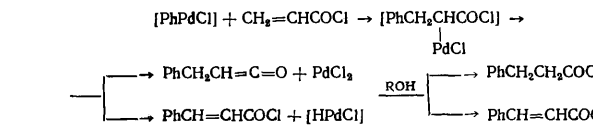
The arylation of olefins with functional groups has also been achieved. If a complex containing in the β-position relative to the metal a group tending to form an anion is formed in the interaction between the substituted olefin and the organopalladium compound, the decomposition of this complex can proceed with elimination of the corresponding anion instead of the hydride. For example, in the arylation of allyl halides the intermediate organopalladium compound decomposes exclusively with the elimination of the chloride ion[9]:



Aryl groups with various substituents (the nitro-group and ether and aldehyde groups) were introduced in this way into the allyl position. On the other hand, when the ferrocenyl group is introduced into allyl chloride, palladium hydride is split off and not the chloride[27]:

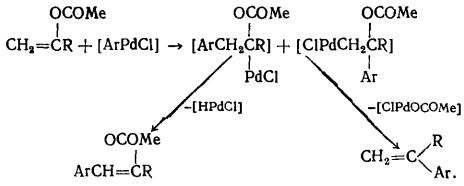


Arylation of the chlorides of αβ-unsaturated acids in the presence of $PdCl_2$ led to the formation of a mixture of various products[30]:

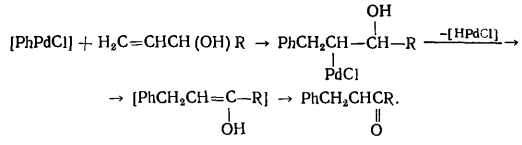


Depending on the pathway in the decomposition of the organopalladium complex, with elimination of $PdCl_2$ or [HPdCl], esters of β-phenylpropionic or substituted cinnamic acids are formed in the subsequent alcoholysis. However, the yields of both are low, of the order of 10 to 16%, so that the reaction in this form has no preparative interest.

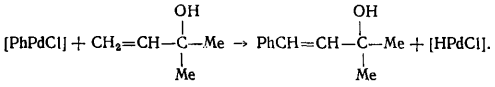
The reaction of enol ethers and esters with arylpalladium salts, obtained *in situ*, gives rise to various products, depending on the mode of addition of the organopalladium compound (see p. 556) and on the nature of the species eliminated[10]:



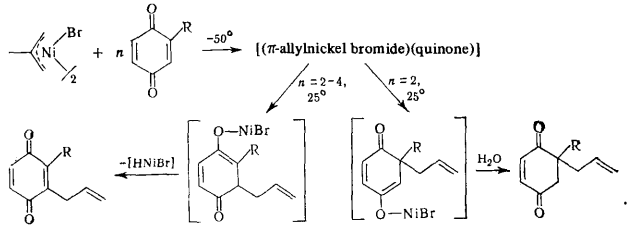
In certain cases the arylation reactions of substituted olefins are accompanied by rearrangements. For example, phenylation of primary or secondary allyl alcohols leads to 3-aryl-substituted aldehydes and ketones, probably via the corresponding enols[8]:



Tertiary ally alcohols react normally:



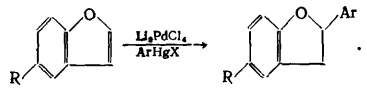
Examples of the introduction of substituents into benzo- and naphtho-quinones with the aid of Group VIII metal complexes are now known. The reaction of π-allylnickel bromides with *p*-quinones, discovered by Hegedus et al.[31], which makes it possible to introduce an allyl substituent into the quinones, is of great interest. The synthesis is carried out in polar solvents, [tetrahydrofuran (THF), dimethylformamide (DMF)] in two stages. Mixed allyl–quinone π complexes of nickel are formed at a low temperature (−50°C), while the second stage takes place at room temperature. In particular, coenzyme Q_1 and 1-plastoquinone were obtained by this method in 40 and 30% yields respectively. The authors represent this reaction by the following general scheme:



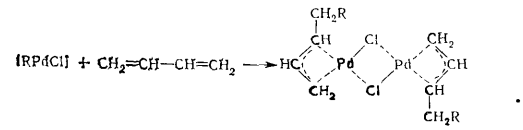
Thus the reaction with a monosubstituted *p*-benzoquinone results in the formation of a mixture of isomeric allylquinones and, for a comparatively small quinone: nickel complex reactant ratio cyclohexenedione derivatives are also formed. In the first two stages 1,4-addition probably takes place. However, the third stage suggested by the authors—the elimination of the hydride—appears unlikely; the oxidation of the cyclohexadienone derivative by an excess of the initial quinone is more probable.

Kim et al. [32] found that *p*-quinones can be methylated by methylpalladium complexes obtained *in situ* from a palladium salt and a methylcobalt chelate. In the methylation of *p*-benzoquinone the yield is very low (4%); but in the case of 1,4-naphthoquinone it is much higher (30–40%). The palladium salt can be replaced by a nickel salt, although the yield is then appreciably reduced.

The unsaturated systems capable of being arylated include certain heterocyclic compounds [33]. The interaction of benzofuran with intermediate arylpalladium chloride leads to the formation of 2-arylbenzofuran derivatives:

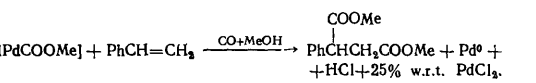


Conjugated dienes such as butadiene and cyclohexa-1,3-diene react with alkyl-, aryl-, and ferrocenyl-palladium compounds obtained *in situ*, with formation of stable allyl π complexes [12, 34]:

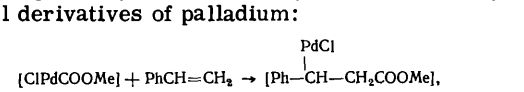


Methyl 5-ferrocenylsorbate was obtained directly from methyl sorbate and ferrocenylpalladium chloride, evidently also via an allyl π intermediate.

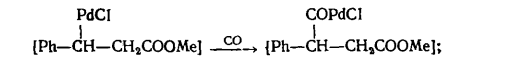
Reactions involving the insertion of simple molecules, particularly CO, in the palladium–carbon bond in the intermediate organopalladium σ compounds give rise to extensive synthetic possibilities. We shall quote several examples of reactions of this kind. Thus Heck discovered the reaction involving the addition of two methoxycarbonyl groups to multiple bonds [35]. When olefinic and acetylenic hydrocarbons are acted upon by methoxycarbonyl derivatives of palladium [obtained directly from $PdCl_2$, methanol, and CO or by the double decomposition reaction of palladium(II) with the corresponding organomercury compound], dialkoxycarbonyl derivatives are formed:



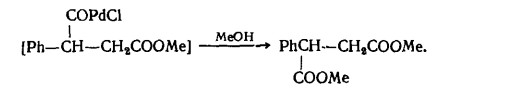
The olefin probably reacts initially with the methoxycarbonyl derivatives of palladium:



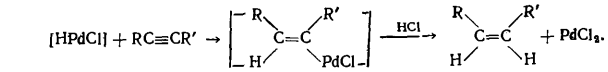
and then a CO molecule is inserted in the new palladium–carbon bond:



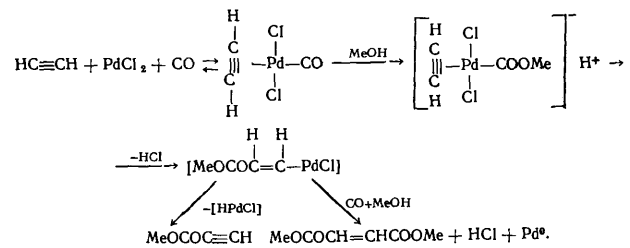
after this, the organometallic compound undergoes alcoholysis:



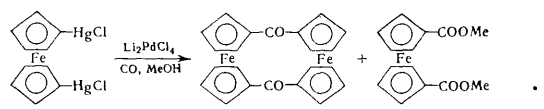
In the reactions with acetylene the yields of the products exceed the stoichiometric values (up to 200%), which can be accounted for by the regeneration of the palladium(II) compound as a result of the oxidation of zero-valent palladium by acetylene:



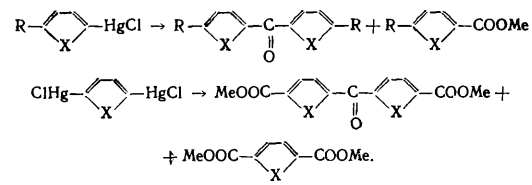
Overall, the reaction with acetylenes can be represented as follows:



The carbonylation of 1,1′-bis(chloromercury)ferrocene with the aid of a palladium salt in methanol at 70°C and a CO pressure of 50 atm led to the synthesis of 1,1-ferrocenophane-1,12-dione [36]:



The carbonylation of organomercury derivatives of the furan and thiophen series was achieved by means of the same scheme [37]:

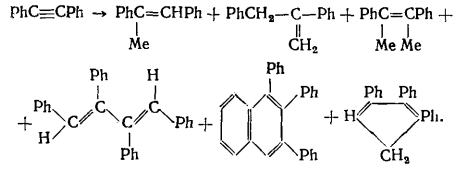


Generalising the reactions discussed in the present section, in which olefins are alkylated and arylated by organic σ derivatives of transition metals, obtained by double decomposition reactions of organic derivatives of non-transition metals with Group VIII metal salts, one may conclude that this procedure has great possibilities for the synthesis of a wide variety of derivatives of unsaturated compounds.

In all the reactions examined the intermediate formation of transition metal σ complexes is postulated, but these complexes cannot be isolated in view of their high kinetic lability. There exists only indirect evidence for their formation. In particular, in a study of the alkylation of olefins by organic derivatives of chelate complexes of cobalt in the presence of palladium compounds it was possible to isolate bis-π-allylpalladium chloride, formed as a result of the double decomposition reaction between the allyl derivative of the cobalt chelate and palladium(II). [26] Presumably the allyl π complex is formed on rearrangement of the intermediate π-allylpalladium chloride.

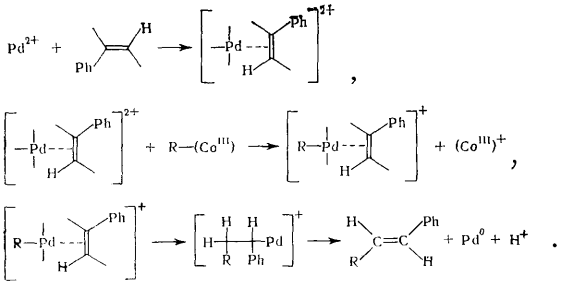
The reaction of the methyl σ complex of rhodium $MeRh(PPh_3)_3$ with diphenylacetylene can serve as an example of the alkylation of an unsaturated compound by a more stable organic σ derivative of a transition metal.

It results in the formation of the same products as in the alkylation of tolane by MeMgBr in the presence of $RhBr_3 \cdot 3H_2O$, $Rh(PPh_3)_3Br$, or $(PhCN)_2Pd$ [15,16]:



The main product is α-methylstilbene, with the additional formation of isomerisation, dimethylation hydrogenation, and cyclisation products.

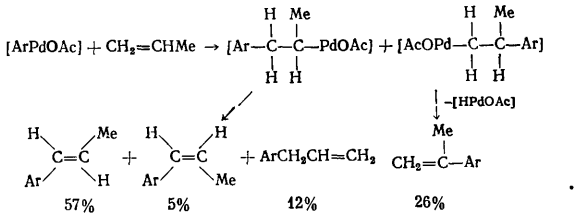
The mechanism of the intermediate formation of organopalladium σ compounds, has been studied in relation to the interaction of palladium complexes with organic derivatives of chelate Group VIII metal complexes of olefins, where this stage is apparently rate-limiting[38]. It was shown that the dealkylation of methylcobalamine by lithium chloropalladate in the presence of styrene proceeds approximately fifty times faster than in its absence. Evidently the stage involving the transfer of the organic ligand from cobalt to palladium precedes the formation of the π complex of palladium with the olefin. The next stage is apparently the exchange proper of the organic group between the organometallic compound and the olefinic π complex of palladium, the influence of the olefinic ligand in the π complex promoting the labilisation of the Pd–Cl bond in the *trans*-position relative to it:



The observed electronic effects in the reactions considered correspond to the usual rules governing electrophilic substitution at a metal atom.

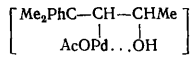
Later a study was published in which the kinetics of the transfer of the methyl group from methylcobalamine to palladium(II) were investigated in the absence of any organic substrate[39]. The reaction products were aquocobalamine, metallic palladium, and methyl chloride. In discussing the reaction mechanism, the authors also suggest the intermediate formation of a methylpalladium σ complex as a result of electrophilic attack by Pd^{2+} on the carbon atom linked to cobalt.

In studies of the arylation and alkoxycarbonylation of olefins by organopalladium compounds factors on which the mode of addition of the organic group to the olefin depends were determined[40,41]. It was found that in the main the reaction mechanism is determined by steric factors, namely the large organic group adds preferentially to the less substituted carbon atom involved in the double bond and palladium therefore adds to the more substituted carbon atom. When the steric and electronic factors act in the same direction, the reaction becomes fairly selective. For example, in the methylation of styrene by "methylpalladium acetate" 95% of trans-β-methylstyrene, about 3% of the *cis*-isomer, and only 2% of α-methylstyrene is obtained. In the arylation of propene the steric and electronic factors act in opposition. The principal mode of substitution is in this case determined by steric effects:

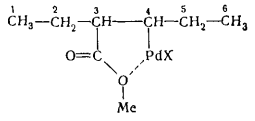


However, the ratio of the yields of products shows that the electronic effects are nevertheless manifested quite distinctly.

In cases where there is a possibility of the formation of a chelate intermediate, this implies a significant influence on the mode of the reactions under consideration. This effect is observed in the arylation reactions of allyl alcohols which we have already discussed[8]. The addition of the phenyl group to such alcohols takes place preferentially at the terminal carbon atom involved in the double bond of the alcohol. This cannot be accounted for either by electronic or steric effects. The mode of addition is in this case probably determined by the possibility of the formation of the four-membered ring

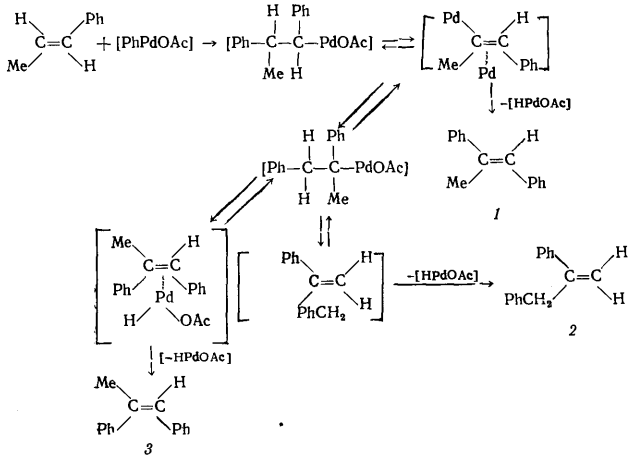


in the intermediate organopalladium compound. The same effect is manifested in the methoxycarbonylation of cyclic olefins and olefins with an inner double bond, leading to preferential substitution in the allyl position. For example, in the methoxycarbonylation of *trans*-hex-3-ene the following chelate intermediate may be formed:



Evidently the *cis*-elimination of the hydride from the 3-position in this complex cannot occur.

Identification of the products obtained in the reaction of "phenylpalladium acetate" with *trans*-1-phenylprop-1-ene yielded information about the stereochemistry of the reaction:

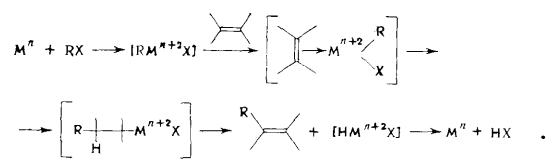


The reaction results in the formation of a mixture of olefins with a nearly quantitative overall yield. The principal product is *trans*-1,2-diphenylprop-1-ene (*1*) (98% yield) with the additional formation of 2,3-diphenylprop-1-ene (*2*) (0.5% yield) and only traces of *cis*-1,2-diphenylprop-1-ene (*3*). The formation of the *trans*-isomer corresponds to the mechanism involving the *cis*-addition of [PhPdOAc] to propenylbenzene with the *cis*-elimination of [HPdOAc]. The preferential formation of *trans*-1,2-diphenylprop-1-ene might be accounted for also with the aid of the *trans*-addition–*trans*-elimination mechanism. However, this appears unlikely[3,40,41], since the reaction should then proceed intermolecularly and not in the inner coordination sphere of palladium.

The selectivity of the substitution of the vinyl hydrogen atom in olefins is significantly influenced by the nature of the anion in the initial palladium complex. The selectivity increases on replacement of the chloride ion by the acetate ion[40,42,43]. It was established that the use of chlorides induces the isomerisation of olefins (both the migration of the double bond and *cis–trans* isomerisation). This can probably be explained by the greater stability of the complex [HPdCl] compared with [HPdOAc]. There is probably sufficient time for the hydride complex [HPdCl] to add several times to the double bond and to be split off before its decomposition into zero-valent palladium and HX. Such partial reversibility of the elimination of the hydride leads to a decrease of selectivity, namely to an increase of the yield of the thermodynamically more stable isomer.

III. ALKYLATION AND ARYLATION OF OLEFINS BY ORGANIC HALOGENO-DERIVATIVES IN THE PRESENCE OF GROUP VIII METAL COMPOUNDS

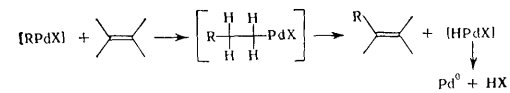
The studies carried out in recent years have shown that not only organometallic compounds but also purely organic reagents, in particular organic halogeno-derivatives, can serve as donors of the alkyl and aryl groups in olefin substitution reactions carried out with the aid of transition metal compounds. The possibility, in principle, of achieving such reactions is based on the ability of metals in a low oxidation state to enter into oxidative addition reactions and on the ability of the resulting complex to interact with the olefin:



Catalytic reactions involving the substitution of the vinyl hydrogen atom of olefins by aryl, benzyl, and styryl halides with the aid of palladium have now been achieved[44–46]. These reactions are carried out in methanol[44,45] or without a solvent[46] at 100°C and atmospheric pressure. The active catalysts are zero-valent palladium and palladium(II) salts. In the latter case the reaction probably begins with the reduction of palladium(II) to zero-valent palladium under the influence of the olefin or methanol. This is followed by the oxidative addition of the organic halogeno-derivative to the zero-valent palladium. The observed reaction rate is determined by the rate of this stage. The reactivity of aryl halides varies in the sequence PhI > PhBr ≫ PhCl, which corresponds to the change in the bond energy between carbon and halogen. The interaction results in the formation of an organopalladium σ complex:

$$Pd^0 + RX \rightarrow [RPd^{II}X].$$

The subsequent interaction of this complex with the olefin leads to the formation of a substituted olefin and the unstable palladium hydride:



The zero-valent palladium is involved in the next reaction cycle.

The accumulation of HX in the reaction medium has an inhibiting effect on the reaction. The point is that the σ complex [RPdX] is unstable in relation to the action of acids; it can be split into RH and PdX_2. Furthermore, an acid medium promotes the hydrogenation of olefins. For this reason, various bases are used to bind HX: potassium acetate and benzoate, pyridine, triethylamine[44,45], and tri-n-butylamine[46].

These reactions are applicable to various substituted olefins containing nitro-, methoxy-, and methoxycarbonyl groups. In the case of olefins containing a methylene group next to the double bond the yields of the reaction products are relatively low[46]. This can be explained by the formation of allyl π complexes of such olefins with the catalysts.

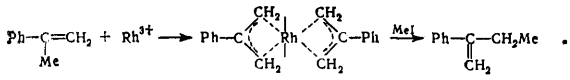
Despite their advantages over arylation, benzylation, and styrylation by organometallic derivatives these reactions also suffer from certain limitations, namely the reaction products are usually a mixture of geometrical isomers, the isomerisation taking place intramolecularly, possibly via a π complex of palladium hydride with the olefin. This is supported by the finding that none of the initial olefins isomerises under the reaction conditions. Since the reaction proceeds at an elevated temperature, the migration of the double bond becomes appreciable. Furthermore, one cannot employ in the reaction starting materials sensitive to the action of bases. This probably explains the failure of the attempts to alkylate olefins by alkyl halides under these conditions.

Olefins were successfuly methylated by methyl iodide in another system using rhodium compounds[47]. The methylation of styrene, linear terminal olefins, and cyclohexene was achieved under the joint action of methyl iodide or chloride or tetramethylammonium iodide and rhodium trichloride in the presence of a reducing agent. The reducing agents used are primary and secondary alcohols and also bivalent tin. Weak bases such as DMF and acetronitrile are used to bind HX in this reaction. Reactions are carried out at 100–160°C using an excess of the olefin. The methylated olefins are formed in stoichiometric yields.

The active species in the reaction is probably a complex of rhodium(I), which is involved in the oxidative addition of MeI. However, this complex is unstable and is partly converted into zero-valent rhodium under the reaction conditions, which was found to be incapable of transferring the organic group to the olefin. This factor complicates the catalytic process.

Together with monomethylated olefins, the formation of small amounts of doubly methylated olefins has been observed in a number of instances. This can be explained

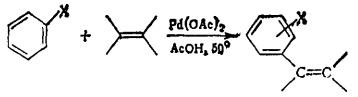
by the subsequent methylation of the allyl π complex of rhodium with the monosubstituted olefin:



IV. ARYLATION OF OLEFINS BY AROMATIC COMPOUNDS IN THE PRESENCE OF TRANSITION METAL SALTS

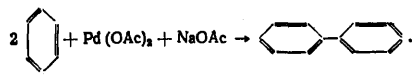
The communications of Fujiwara and coworkers [42, 48, 49] concerning the reactions of olefins with benzene derivatives in the presence of palladium(II) salts, which appeared in 1967, initiated a whole series of investigations on the synthesis of substituted olefins using a wide variety of aromatic compounds as arylating agents.

The interaction of benzene derivatives, an olefin, and palladium acetate results in the formation of aryl-substituted olefins [42, 48, 47]:



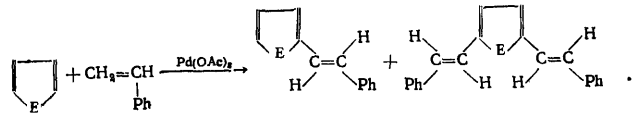
The reactions are carried out with equivalent amounts of the olefin and palladium(II) acetate in a large excess of the aromatic compound in the presence of acetic acid. The reaction does not proceed without the acid. The yield of the arylation products varies from 10 to 90% and metallic palladium is produced. When silver and copper acetates are added to the reaction mixture [50] or the reaction is performed under oxygen pressure [51, 52], it can be made catalytic as a result of the regeneration of palladium(II).

It is noteworthy that the arylation of olefins is accompanied by the dimerisation of the aromatic radicals. The addition of nucleophilic reagents causes the reaction to be of the preformation type and permits its employment for the synthesis of biaryl derivatives [52-61]:



Intramolecular aromatic substitution can also be achieved with the acid of palladium(II). [62] Thus the reaction of the olefins $PhR_2C-CH=CH_2$ (R = Ph or Me) with palladium(II) acetate in acetic acid at 80°C results in the formation of the corresponding 1,1-disubstituted indenes:

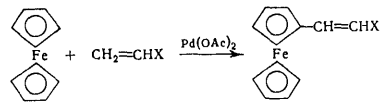
Together with benzene derivatives, other compounds with aromatic properties such as heterocycles [33, 63] and ferrocene [64-66] proved to be active arylating agents. It has been shown that furan, thiophen, selenophen, *N*-methylpyrrole, and *trans*-2-styrylfuran arylate olefins with high yields, disubstituted derivatives being formed together with monoarylated derivatives:



E = O, S, Se.

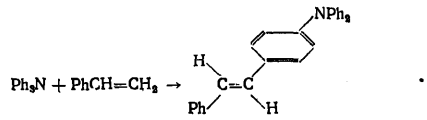
The authors believe that the reaction proceeds in two stages: monosubstituted products are formed in the first stage and further alkenylation takes place in the second stage. This is not observed in the reaction of benzenoid aromatic compounds with olefins [48]. Substitution in heterocycles takes place mainly at the 2- and 5-positions, which corresponds to the usual orientation in electrophilic substitution in heterocycles of this kind.

Ferrocene reacts with various olefins in the presence of palladium(II) acetate with formation of alkenylferrocenes [64-66]. The reactivity of olefins increases appreciably under the influence of electron-donating groups:



(X = Ph, CN, COOMe, CHO)

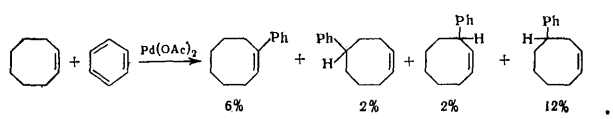
The arylation of olefins by triarylamines is an interesting example of the formation of compounds with functional groups as substituents [24]. The reaction with styrene gives rise to *trans*-*p*-diphenylaminostilbene:



Thus there is a significant difference between the behaviour of Ar_3N as an arylating agent and Ar_3E, where E = P, As, Sb, or Bi; in the presence of the latter stilbenes without a heteroatom are formed (see p. 553). Evidently this difference is due to the greater strength of the C–N bond than the bond between carbon and other Group VA elements.

The aryl group adds to asymmetric olefins preferentially at the least substituted carbon atom involved in the double bond, probably because of the steric hindrance of the substituents [67].

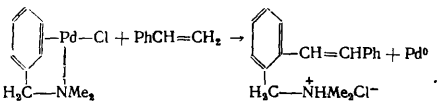
In contrast to acyclic olefins, cycloolefins give rise to a mixture of isomeric arylation products [68]:



The initial stage in the arylation of olefins is probably the formation of an organopalladium σ compound as a result of the direct combination of palladium with a benzene ring [43]:

$$PdX_2 + ArH \rightleftarrows [ArPdX] + HX$$

This is supported by Tsuji's data[69] concerning the formation of an arylated product in the reaction of the stable aryl σ complex between palladium and styrene:



The nature of the substituents in the aromatic system has a significant influence on the mode of substitution in the benzene ring. Electron-donating groups, for example alkyl groups, direct the substituents to the *o*- and *p*-positions, while electron-accepting groups (the nitro-group) are *m*-directing; chlorobenzene gives rise to a mixture of isomeric products with a high content of each isomer[70]. Hence the nature of the substituent hardly affects the reactivity of the aromatic compound.

On the other hand, the presence of polar groups in the olefin has a marked influence on the yields of the arylated products[71]. The reactivity of olefins decreases in the sequence

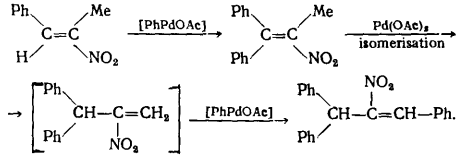
$$PhCH{=}CH_2 > NCCH{=}CH_2 > AcOCH{=}CH_2 > EtOCH{=}CH_2.$$

In arylation with heterocyclic aromatic compounds the inhibiting effect of electron-donating substituents in the olefin is also observed[31].

The reactivity of nitroolefins varies as follows[72]:

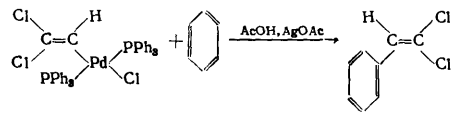
$$PhCH{=}CHNO_2 > CPhCH{=}CPhNO_2 > Ph_2C{=}CHNO_2.$$

It is noteworthy that the phenylation of β-methyl-β-nitrostyrene does not stop at the monoarylated product stage but leads to an olefin with two additional aryl groups[73];

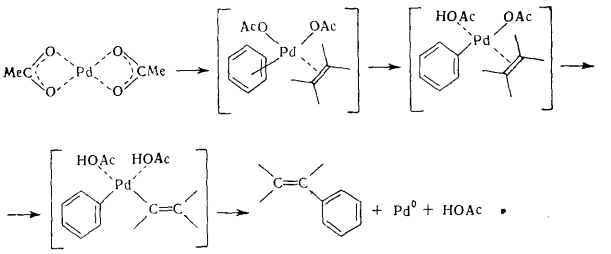


The absence of a substituent effect in the aromatic system on the rate of phenylation shows that the stage involving the formation of the aryl palladium σ complex is probably not rate-limiting. On the other hand, the marked influence of the substituents in the olefin suggests that the slow stage is the interaction of the olefin with palladium. However, the problem of the rate-limiting stage remains controversial. Thus the formation of an arylpalladium σ complex is believed[74] to be the rate-determining stage. This assertion is based on a study of the isotope effect in the arylation of olefins by deuteriobenzene in the presence of palladium(II) acetate.

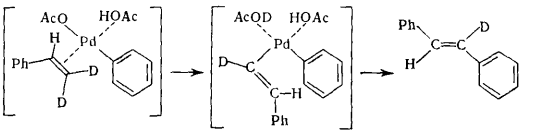
It has been suggested[71] that alkenylpalladium σ complexes take part in the arylation of unsaturated systems together with arylpalladium σ complexes. This is confirmed by the reaction of a stable vinylpalladium σ complex with benzene or toluene, which leads to the formation of an arylated olefin[75]:



Thus the mechanism of the reactions considered can be represented as follows[71]:



Indeed the study of the arylation of olefins in the presence of palladium using isotopes showed that, in contrast to the oxidation of olefins, there is no hydride shift in this reaction[76,77].



A similar study showed that the arylation of olefins by heterocyclic aromatic compounds also takes place without a hydride shift[33]. On the other hand, the mechanism of the substitution of unsaturated compounds with ferrocene includes a hydride shift stage[66].

The methods for the alkylation and arylation of olefins described above have been available for only a few years but they are nevertheless already of considerable preparative interest. Furthermore, the study of these reactions yields interesting information about the role of the formation of organometallic π and σ compounds in homogeneous catalysis.

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Ethereal Electrolytes for Aluminium Plating

A.Levinskas

The review deals in detail with ethereal electrolytes widely used at the present time for the formation of high-quality aluminium coatings and mandrels at room temperature. The most important postulates of the theory of electrode processes in ethereal media are discussed on the basis of the latest classification of ethereal electrolytes. The industrial applications of electrolytic aluminium-plating processes and prospects for their further development are briefly enumerated. The bibliography includes 106 references.

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I. INTRODUCTION

Aluminium electroplating yields coatings and electroforming mandrels having a wide variety of physicomechanical properties and at the same time capable of meeting the complex requirements demanded of such coatings by modern instrument engineering, electrical engineering, radio electronics, space technology, and optics. The applications of ethereal electrolytes operated at room temperature are the most promising. In the last decade they have been used in a number of technological processes and industrial technological developments. The experience gained in the employment of ethereal electrolytes enriched the electroplating technology by fundamentally new procedures for electrodeposition in hermetically sealed electrolysers. Furthermore the group of ethereal electrolytes for aluminium platings is the object of current electrochemical studies. Numerous data on the compositions and chemical, electrolytic, and physicochemical properties of ethereal electrolytes and on the characteristic features of electrocrystallisation involving non-aqueous media have now accumulated. All these data refer, in Bockris's terminology[1], to the ionics and electronics of non-aqueous solutions and liquid phases, i.e. important branches of modern electrochemistry.

The review deals systematically with all the known ethereal electrolytes for aluminium plating and describes the most important results of their electrochemical study.

II. ETHEREAL AMINE AND ETHEREAL HYDRIDE ELECTROLYTES

One of the early studies on ethereal electrolytes for aluminium plating was the development of the ethereal amine baths by Doumas and Murphy[2,3]. The general composition of ethereal amine electrolytes may be characterised by the following proportions of the initial components used to prepare the electrolyte: anhydrous aluminium chloride (on average 10–45 mole %), an alkylamine including up to three alkyl groups and up to twelve carbon atoms in the molecule (20–40 mole %), and an aliphatic ether incorporating up to six carbon atoms (30–80 mole %). The electrolytes are prepared by adding, with stirring, the ethereal aluminium halide solution to the cooled amine diluted with the ether. According to the authors, refined electrolytic aluminium is deposited over a wide range of cathodic current densities (up to 0.130–0.140 A cm^{-2} inclusive), but preliminary treatment with a current is necessary. The working temperature of the ethereal amine baths is mainly 20–30°C. The gas used to produce the hermetic seal is dry nitrogen or argon. Best results were obtained for electrolysis in electrolytes prepared using the following components: n-butylamine, ethylhexylamine, and diethyl, dipropyl, and butyl ethyl ether or tetrahydrofuran.

Brenner frequently noted the unsatisfactory reproducibility of the composition of ethereal amine electrolyte. Menzies and Salt[4] subsequently showed that the reproducibility is fully ensured only when chemically pure components and anodes of specially pure aluminium are employed. The authors improved the technology of the preparation of ethereal amine baths before use and the procedures for their employment, as a result of which high-quality elastic aluminium deposits were obtained with thicknesses up to 1–2 mm with an average current yield of 78–80%. Consequently ethereal amine electrolytes are suitable both for electroplating and galvanoplastics.

The development of an NBS (U.S. National Bureau of Standards) process by Brenner, based on his ethereal hydride bath, has had a considerable influence on the development of research into ethereal electrolytes for aluminium plating[5–9]. The composition of the ethereal hydride electrolyte, expressed in terms of the concentrations of the initial components was as follows: 1–4 M anhydrous aluminium chloride, 0.5–1.0 M lithium hydride or 0.1–0.4 lithium tetrahydroaluminate, and absolute diethyl ether. The electrolyte was made by mixing the components in different ways, but in all cases the optimum conditions for the Wiberg–Schlesinger reaction must be maintained[10].

The ethereal hydride electrolyte has excellent electroplating properties. The aluminium deposit contains only traces of heavy metals. A deposit 20–25μm thick is continuous, cryptocrystalline, and elastic. These qualities as well as the 100% current yield of aluminium are maintained at different rates of electrocrystallisation up to values of the order of 0.10–0.15 A cm^{-2} inclusive.

Galvanoplastic layers up to 2–5 mm thick can also be obtained using the NBS electrolyte. Special electroforming procedures make it possible to vary the actual thickness of the mandrel. The NBS ethereal hydride electrolyte is usually hermetically sealed under dry nitrogen or argon. The exposure of its surface to air during the replacement of the electrode rods must be reduced to a minimum. When the requirements of an effective hermetic seal, regular filtration, adjustment, and periodic replacement of the spent anolyte are observed, continuous operation of the bath around room temperature is possible for 15–18 months. Brenner proposed also other ethereal hydride electrolytes, the components of which are sodium or potassium hydride, fused aluminium bromide, butyl ethyl, dibutyl, and diphenyl ethers, anisole, phenetole, etc.[11] However, cathodic deposits of the highest quality and the highest operating efficiency of the baths were achieved only in the NBS process.

The successful development of the ethereal hydride electrolyte for aluminium plating enabled Brenner to turn subsequently to the study of the possibilities of the preparation of analogous hydride systems. Thus they obtained titanium–aluminium, titanium–zirconium, beryllium–boron, magnesium–zirconium, magnesium–titanium, and magnesium–beryllium alloys from an ethereal hydride–tetrahydroborate electrolyte and beryllium–aluminium and magnesium–aluminium alloys from an ethereal hydride electrolyte[12–14]. Subsequently the method for the preparation of the beryllium–aluminium alloy was improved by Lui and Guidotti[15]. It is noteworthy that all cathodic deposits of the above alloys are formed in the form of a powder or strained coatings. Therefore the method of their electrodeposition is of extremely great theoretical value.

Certain electroplating problems of the NBS process have been examined also in studies by other investigators. A microscope study of the structure and properties of the aluminium deposit as a function of its thickness and the nature of the cathode material was carried out by Elze et al.[16] The changes in the morphology, texture characteristics, and microhardness of the deposits after a prolonged operation of the bath (up to 1200 Ah) were studied with the aid of an electron microscope by Addison et al.[17] The high purity of the aluminium deposit obtained from an ethereal hydride electrolyte was confirmed spectroscopically and by X-ray diffraction in studies of Hayashi and Ishida[18,19], while Takahashi and Nomura improved the conditions for the attainment of optimal electrolysis conditions[20].

The need for the improvement of the operating conditions of ethereal hydride baths led to the creation of the so called modified ethereal hydride electrolytes for aluminium plating. McGraw[21] and subsequently Smith and McGraw[22] proposed an "involatile" hydride electrolyte with an ignition point increased to 85–90°C (the Lovet electrolyte). Compared with the ethereal hydride NBS electrolyte, the Lovet electrolyte contains only a very small proportion of diethyl ether in a free state. The presence of alane complexes in the Lovet concentrate requires very careful protection of the latter from atmospheric carbon dioxide. A disadvantage of the Lovet electrolyte is a somewhat reduced conductivity $(0.7–0.8) \times 10^{-3}\ \Omega^{-1}\text{cm}^{-1}$, so that an increased potential is needed. Subsequently special ionising additives were selected and synthesised. The most effective is 2-ethoxyethyltrimethylammonium chloride, the addition of which to the Lovet electrolyte increases its conductivity to $(0.1–0.2) \times 10^{-1}\ \Omega^{-1}\ \text{cm}^{-1}$. A variant of the modified Lovet hydride electrolyte (the Etmac electrolyte) with an enhanced conductivity was proposed by McGraw and improved by Beach and coworkers[23,24]. The aluminium deposit obtained in the Etmac electrolyte is less elastic and its microhardness is almost twice as high as the average microhardness of electrolytic aluminium.

A group of modified ethereal hydride electrolytes with a more complex composition was developed by Japanese investigators—Ishibashi, Hanamura, Yoshio, Kurata, and others[25–32]. The composition of the electrolytes was based on the optimum ratio of the volume fractions of the ether (tetrahydrofuran or its derivatives—2,3-dichlorotetrahydrofuran, 3-chloro-2-methyltetrahydrofuran, 3-bromotetrahydrofuran, 2-methyltetrahydrofuran, and 2,2-dimethyltetrahydrofuran) and the hydrocarbon (benzene, chlorobenzene, toluene, xylene, dichlorobenzene, and chlorotoluene). For example, in one of the variants the set of components of the modified electrolyte contained 58 vol.% of tetrahydrofuran, 42 vol.% of the hydrocarbon, 0.7–1.0 M aluminium chloride, and 0.2–0.7 M lithium tetrahydroaluminate. The cathodic current density was 0.01–0.05 A cm^{-2}, the experiments were performed at room temperature, the thickness of the coating was up to 0.1 mm, and the purity of the deposit was 99.999 wt.%. The role of the hydrocarbon additive consists in increasing the conductivity. Diethyl, dipropyl, diisopropyl, or dibutyl ethers can be used as other additives and poly(vinyl chloride) or 1,2-dichloroethane can be used as brightening agents. Bright coatings can be obtained in some cases by anodising in the same electrolyte.

The above studies dealt mainly with the solution of problems concerning the composition, preparation, stability, and efficiency of the ethereal electrolytes, the optimal conditions for electrolysis and the principles governing the formation of hermetic seals and adjustment of the baths were established, and the physicomechanical and morphological properties of the aluminium deposits were investigated. Systematic studies on the theory and kinetics of the electrode processes were not made, apart from several investigations on specific problems.

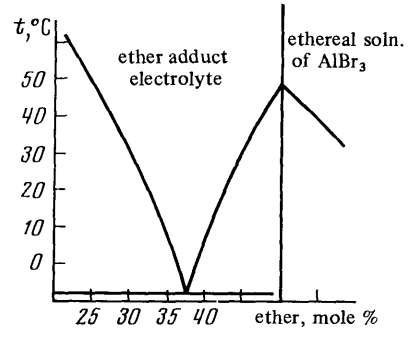

Figure 1. Phase diagram for the aluminium bromide–diethyl ether system.

Connor and Brenner[11] and Clay et al.[33] accumulated extensive factual data on the conductivities of ethereal aluminium halide solutions and an ethereal hydride electrolyte, established the component ratios corresponding to maximum conductivity in the total volume and in the catholyte or anolyte, and investigated the transport of the

hydride component. Using the component ratios thus determined (the ratios of lithium hydride and aluminium halide), the authors put forward suggestions concerning the type of ions promoting the electrocrystallisation of the aluminium deposit. On the basis of a similar correlation between conductivity and composition, Ishibashi and Yoshio[26] attempted to account for the nature of the ionisation of the electrolyte modified with tetrahydrofuran. As mentioned correctly at one time by Kessler et al.,[34] such determinations of the type of ionisation ($Li^+AlH_4^-$, $Li^+AlH_2Cl_2^-$, $Li^+AlHCl_3^-$, etc.) are made without due allowance for the properties of the alane complexes and the nature of the chemical composition and structure of the phases of the ethereal electrolytes.

Individual Tafel relations, obtained in narrow ranges of cathodic current densities, are quoted in reports by Hayashi and Ishida[18,19] and Takahashi and Nomura[20].

III. A NEW CLASSIFICATION OF ETHEREAL ELECTROLYTES

Systematic studies on ethereal electrolytes using a wide variety of electrochemical techniques are being made in our laboratory[35,36]. The objects of the studies are the principal groups of electrolytes: the NBS ethereal hydride electrolyte, the Lovet ethereal hydride electrolyte, ethereal amine electrolytes, and also the etherate, ethereal ammonia, and ethereal dative electrolytes which we proposed. The similarity of their chemical and electrochemical properties is due to the similar proportions of the ingredients in all the groups enumerated.

The etherate of an aluminium halide (chloride or bromide) solvated by the ether constitutes the structural and electrolytical basis of all the phases of the ethereal electrolytes. Diethyl ether is not the only one which can serve, in principle, as the main component of the molecular complex, but it is the most readily available ether, is most convenient to handle, and at the same time ensures the most satisfactory electroplating parameters.

The degrees of solvation of the etherate are various. With an increase in the ether content, a usually slight excess of the so called free ether, which exists in all ethereal electrolytes with the exception of the etherate electrolytes, arises relative to the ether involved in solvation[37].

The next ingredient important for the preparation of ethereal electrolytes (with the exception of those of the etherate type) is a substance (or a set of substances) binding vigorously protons, which are weakly solvated by the ether. This ingredient consists of (a) certain organic bases with high acid dissociation constants, which largely exhibit an n-donor (dative) activity—pyrrolidine, hexamethyleneimine, piperidine, ethylaminocyclohexane, morpholine, N-methylmorpholine, benzimidazole, and indole (ethereal dative electrolytes[38]) and n-butylamine, diethylamine, and triethylamine (ethereal amine electrolytes[39]), (b) ammonia (an ethereal ammonia electrolyte[40]), and (c) the hydride mixture (HM), i.e. the set of products of Wiberg–Schlesinger reaction (alane complexes)[41-48] obtained under the conditions of the preparation of ethereal hydride electrolytes (NBS, Lovet, and Etmac electrolytes[49-53]).

The combination of the above ingredients is important for the attainment of the optimal operating conditions in ethereal electrolytes.

IV. FUNDAMENTALS OF THE THEORY OF ELECTRODE PROCESSES IN AN ETHERATE MEDIUM

Aluminium halide-ether is a 1 : 1 molecular adduct of the highly acidic vacant-orbital acid AlX_3 and diethyl ether as the n-donor: $AlCl_3.(C_2H_5)_2O$.ether and $AlBr_3.(C_2H_5)_2O$. .ether ("ether" is the part of the ether involved in solvation). Compared with other bases, diethyl ether exhibits one of the most intense dative interactions in relation to AlX_3.

The thermochemical characteristics are as follows; the heats of formation of the molecular complexes (in the crystalline state) are ΔH_f(cryst.) = −18.6 ± 0.2 kcal mole^{-1} for $AlCl_3.(C_2H_5)_2O$ and ΔH_f(cryst.) = −23.2 ± 0.2 kcal mole^{-1} for $AlBr_3.(C_2H_5)_2O$; the heat of formation of $AlCl_3.(C_2H_5)_2O$ is ΔH_f = −247.91 ± 0.95 kcal mole^{-1} and the heat of formation of the $AlCl_3$ acceptor itself is ΔH_f = −170.77 ± 0.25 kcal mole^{-1}.[54-58]

The high stability of aluminium halide-ether has been confirmed by studies on the physicochemical phase diagrams for the binary[59] and ternary[60,61] systems and also spectroscopically[62]. Thus the characteristics of the electrode processes in ethereal electrolytes should be determined essentially by the electrolytic properties and the nature of the ionisation of the etherate, while the effect of the remaining ingredients is indirect. According to a thermochemical calculation and infrared spectrophotometric and Raman spectroscopic data for the crystalline state and infrared spectrophotometric and ^1H NMR data for the solutions[34,62-66], the type of ionisation of the etherate (and certain related molecular complexes) is determined by the thermodynamically favourable stable tetrahedral structure of AlX_4^- and the competitive interaction of the Al–O and Al–X bonds (dative bonds):

$$AlI_3 \cdot \text{ether} + AlI_4^- . \qquad (1)$$

Allowance for the dimerisation of aluminium halide in melts and solutions leads to a similar scheme:

$$Al_2I_6 \cdot \text{ether} + Al_2I_7^- . \qquad (2)$$

The etherate electrolytes (the region of melts to the left of the dystectic above the liquidus line on the phase diagram for the aluminium bromide-diethyl ether[67]) is the structurally simplest electrochemical system among ethereal electrolytes. The dystectic (Fig. 1) corresponds to the equimolar composition of the complex $AlBr_3.(C_2H_5)_2O$. The specificity of the composition of etherate electrolytes consists in a complete absence of n-donor additives and free ether; the molecules of the etherate are subject to the ionising action of homopolar aluminium bromide dimers[68,69]. It is noteworthy that the region to the right of the dystectic corresponds to the ethereal solution of aluminium bromide (the etherate in an excess of free ether)–the initial mixture for the preparation of all remaining ethereal electrolytes.

When ionisation of types (1) and (2) occurs in the etherate electrolyte, the stages involving the electrodeposition of aluminium in the presence of Al_2Br_6 as the active acceptor are as follows: reduction of the complex cation with liberation of the unstable Br^- ions and free ether molecules; addition of Br^- to Al_2Br_6 with formation of the particularly stable $AlBr_4^-$ structure; addition of ether to Al_2Br_6; transfer of $AlBr_4^-$ from the cathodic region; transfer of $AlBr_n.\text{ether}^{(2/n)+}$ ions (n = 1 or 2) to the cathode. This results in a redistribution of the substance in the electrolyte (in the presence of a membrane between the catholyte and anolyte)—ether is transferred by the solvated cations to the catholyte. The transfer of

ether decreases the density of the catholyte (the isothermal transition to the left of the dystectic implies an increase in the density of the melts—Fig. 1). The coefficients of the variation of the density of the working electrolyte with time are $\Delta\rho = -0.025$ g cm^{-3} per ampere-hour (catholyte) and $\Delta\rho = 0.021$ g cm^{-3} per ampere-hour (anolyte). The stages involving the addition of the decomposition products of the complex cation to Al_2Br_6, unhindered by steric effects, are more distinctive on increase of temperature and on increase of the content of the free acceptor. Such a change in the conditions governing the reduction of the cation reduces the aluminium overvoltage, which is clearly indicated by the constant-resistance polythermal cathodic polarisation plots (Fig. 2). The decrease in the content of the Al_2Br_6 acceptor should somewhat increase the contribution of the diffusion-dependent rate-limitation of the cathodic process, since the enrichment of the surface layer of the electrode in ether at the instant of the reduction of the cation becomes more distinct under these conditions. The effective activation energy for the cathodic process diminishes correspondingly (Table 1).

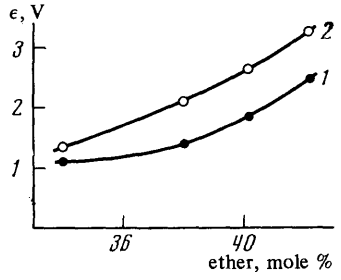

Figure 2. An example of constant-resistance polythermal cathodic polarisation plots for a liquid gallium electrode: 1) electrolyte specific conductance $\kappa = 2.0 \times 10^{-3}\ \Omega^{-1}\text{cm}^{-1}$; 2) electrolyte specific conductance $1.5 \times 10^{-3}\ \Omega^{-1}\text{cm}^{-1}$; $i_C = 0.02$ A cm^{-2}; temperature range 25–50°C.

Table 1. The effective activation energies for the cathodic process (kcal mole^{-1}).

ϵ, V	Ether, mol %				ϵ, V	Ether, mole %			
	41	38	36	32		41	38	36	32
2.00	5.6	7.1	7.8	8.0	2.95	4.8	5.7	6.2	6.9
2.48	5.5	5.8	6.4	7.1	3.43	4.5	5.1	5.3	6.4

The ether molecules arising at the cathode surface interact in a complex manner with the electrolyte. After the enrichment of the electrode surface in ether, the latter adds to Al_2Br_6 or to cations the inner sphere of which may contain several molecules of the base. The interaction with the cations begins to predominate when the concentration of the Al_2Br_6 acceptor in the electrolyte falls. The capture of ether molecules by the inner sphere of the cation increases structural strain. Consequently the reduction of such a cation is facilitated and the rate of the process increases at a constant potential. This conclusion has been confirmed experimentally (Fig.3): the hysteresis polarisation branch as a rule lies above the forward branch, since the cations acquire an additional activity in the region of the reversal of the potential scan. Fig. 3 illustrates the increase of the current by the section *ao* or *cd* ($\Delta i_C > 0$). Δi_C increases with temperature ($\Delta i_C/\Delta t = -0.00023$ A cm^{-2}) and with increase of the Al_2Br_6 concentration in the electrolyte (Table 2).

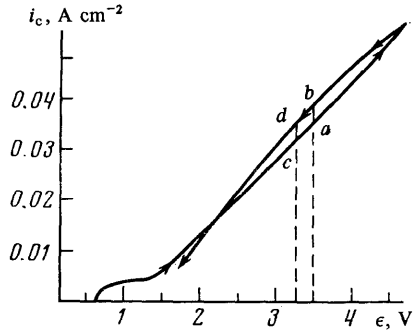

Figure 3. Cathodic polarisation curve for a copper electrode; electrolyte—38 mole % of ether; scan—2.0 V min^{-1}; $t = 20$°C (reference electrode—platinum).

Table 2. The increment of the hysteresis branch Δi_C (A cm^{-2}) ($t = 20$°C; 2V min^{-1} scan; copper electrode).

Compn. of electrolyte, mole % of ether	Δi_C	
	ϵ = 3.25 V	ϵ = 3.50 V
40	0.54	0.47
36	0.47	0.40
31	0.33	0.22

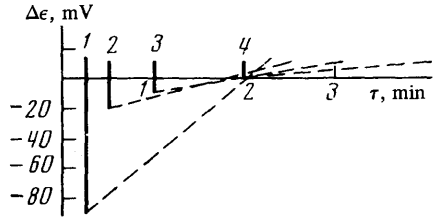

Figure 4. Variation of the probe cell potential after switching off the current pulse: 1) after the first (15 s) pulse; 2) after the second (30 s) pulse; 3) after the third (1 min) pulse; 4) after the fourth (2 min) pulse; continuous lines—variation of Δϵ at the instant of switching off the current pulse; dashed lines—return to the initial potential; copper cathode; $i_C = 0.02$ A cm^{-2}; electrolyte—38 mole % of ether; $t = 20$°C.

The inner sphere of the cation contains together with ether up to two electron-donating Br^- ions, which, having been liberated in the overall electrode reaction and having reacted with the acceptor molecule, stimulate the anodic flux of $AlBr_4^-$ (or $Al_2Br_7^-$) ions. At the instant when the

cathodic current pulse is switched off the increase of the surface $AlBr_4^-$ concentration is manifested by a negative shift of the potential of the platinum probe. In view of the occurrence of the slow reaction between the added free Br_2 and Al_2Br_6, the effect is weaker in subsequent current pulses (Fig. 4).[70,71]

The weak supporting electrolyte in ethereal electrolytes limits the anodic polarisation curve to a single horizontal section located directly beyond the Flade potential (Fig. 5). A passivating film, which is at the same time soluble in the electrolyte is formed along section *bcd*. When this film is observed visually, the anolyte is at the same time seen to be coloured brown. The changes in the electron surface can be compared with the following mechanism for the oxidation of the $AlBr_4^-$ (or $Al_2Br_7^-$) anion:

$$AlBr_4^- - e = AlBr_{3(film)} + \frac{1}{2}Br_2. \qquad (3)$$

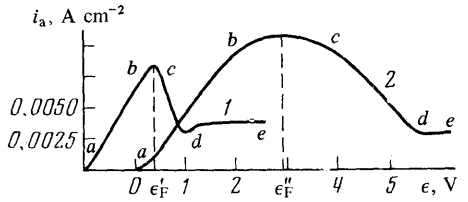

Figure 5. Anodic polarisation curves for aluminium (curve *1*) and platinum (curve *2*) electrodes in an etherate electrolyte.

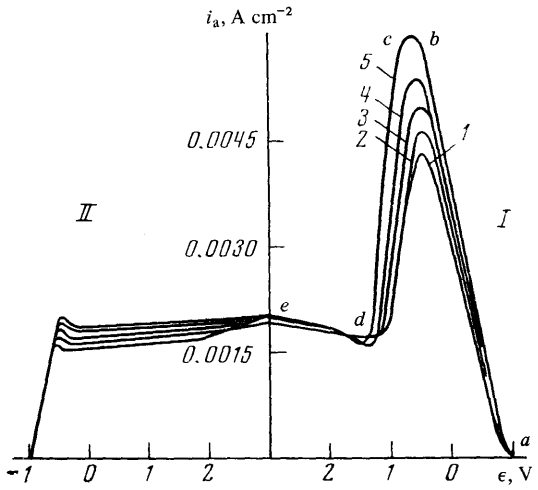

Figure 6. Anodic polarisation curves for an aluminium electrode; electrolyte—31 mole % of ether; scan—2.0 V min^{-1}; t = 25°C: I) forward branch; II) hysteresis branch; rate of rotation of disc electrode (rev. min^{-1}): 1) 400; 2) 800; 3) 1200; 4) 1600; 5) 2000.

Since Br_2 interacts vigorously with aluminium, the colour of the anolyte at the aluminium anode is weaker than at the platinum anode. Owing to the additional Br–Al bonds, the film on the surface of the soluble electrode is more stable, [the passivation maximum is sharper, there are no maxima on the hysteresis branches, and the shape of the polarisation curves changes only slightly when the rate of stirring is altered (Fig. 6)].

Mechanism (3) has been confirmed by studies on the physicochemical properties of the passivating film and on the colour of the surface layer at the anode.

Together with the characteristic absorption wavelength of the Al–O bond (460 nm), the absorption spectrum of the electrolyte (Fig. 7, curve *1*) usually shows a band corresponding to the Br_2–Al_2Br_6 bond (560 nm). The absorption intensity at 560 nm clearly increases following the addition of bromine to the anolyte. A similar increase of the intensity of the absorption band at 560 nm is observed also under the conditions when the electrolyte becomes brown on passivation of the anode (Fig. 7, curve *4*).

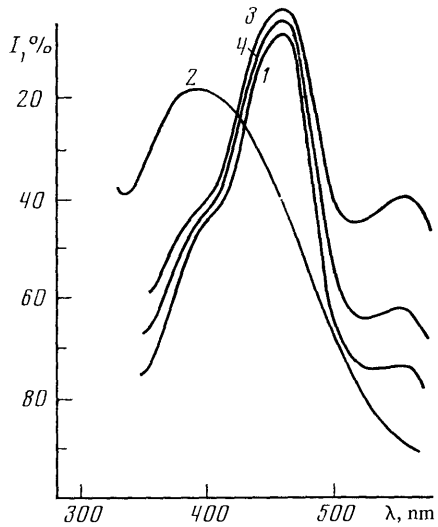

Figure 7. The spectrum of an etherate electrolyte (anolyte): 1) spectrum of electrolyte; 2) spectrum of bromine; 3) spectrum of electrolyte with added bromine; 4) spectrum under the conditions of the brown colour of the electrolyte during the passivation of the anode.

The solubility of the film in ethereal electrolytes of different compositions varies in the same way as the solubility of pure aluminium bromide (Fig. 8). The film dissolves faster in media with a reduced concentration of the free acceptor (Fig. 9). The *bcde* section of the anodic polarisation curve (Figs. 5 and 6) shifts similarly on increase of temperature (0.001–0.004 A cm^{-2} for Δt = 10 degC) or of the rate of stirring. The dissolution of the passivating film in the anolyte (30–32 mole % of ether; volume 30–40 ml) increases its crystallisation temperature on average by 4–5 degC, corresponding to a quantity of electricity of 0.30–0.35 Ah, i.e. displaces the phase equilibrium in the anolyte to the left along the liquidus line (Fig. 1); the same is observed when aluminium bromide is added.

Mechanism (3) for a soluble anode in etherate electrolytes must be supplemented by the indirect dissolution stage

$$\frac{3}{2}Br_2 + Al_{(anode)} = AlBr_{3(film)}. \quad (4)$$

The occurrence of indirect dissolution, which is in general characteristic of the oxidation of anions of the $AlBr_4^-$ type, rules out conditions for the occurrence of disproportionation reactions. At potentials more negative than ϵ_F (Fig. 9) the current yield of the metal in the region of the active electrode surface is almost independent of the rate of stirring (Table 3)[72-74].

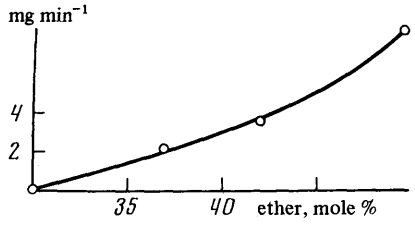

Figure 8. Rate of solution of anhydrous $AlBr_3$ in uniformly stirred etherate electrolytes of different compositions; $t = 50°C$.

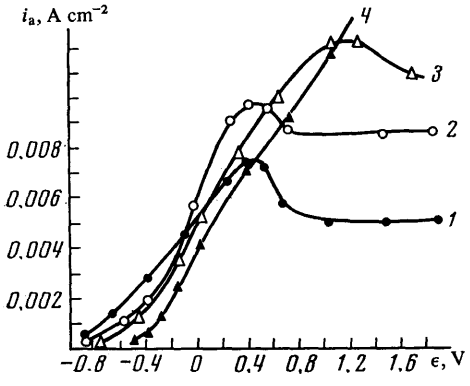

Figure 9. Anodic polarisation curves for an aluminium electrode; amount of ether in electrolyte (mole %): 1) 34; 2) 39; 3) 46; 4) 50.

Table 3. The anodic current yield of aluminium (38 mole % of ether in electrolyte; $i_a = 0.005$ A cm^{-2}; $t = 22°C$).

rev min^{-1}	η_a, %	rev min^{-1}	η_a, %
—	93.5	1000	101.3
600	98.1	1500	106.8

The NBS ethereal hydride electrolyte is structurally most complex among other ethereal electrolytes, since in this case the aluminium halide-ether medium contains the components of the hydride mixture (HM). The composition of the hydride mixture in the range of the initial molar component ratios usually adopted for the electrolyte, $A = LiH : AlCl_3 = 1.40 : 0.25$, varies within fairly narrow limits. If the set of alane complexes is expressed by the molar ratios of the initial monomers $AlHCl_2$, AlH_2Cl, and $LiAlCl_4$ and account is taken of their interaction with the etherate (the mole of the etherate refers by convention to one mole of the monomer), then the typical proportions of the components of the hydride mixture in the etherate medium are readily obtained on the basis of the results of elemental chemical analysis (Fig. 10). The wavenumbers of the absorption bands in the spectra of the electrolyte (534, 492, and 1900 cm^{-1}) correspond to the vibrations of the Al–O, Al–Cl (in $AlCl_2^-$), and Al–H bonds.

The volume of free ether and the ether involved in solvation in the electrolyte is always limited by the total solvating capacity of the etherate medium. For $A > 1.4$ or on direct decrease of the concentration of the etherate (to less than 1 M in terms of anhydrous aluminium chloride) over the ethereal hydride phase, it is possible for an ethereal layer to appear. The separation into layers occurs also following direct dilution of the electrolyte with the ether. The ethereal layer disappears under the influence of the addition of an ethereal solution of aluminium chloride or under the conditions where $A < 1.4$.

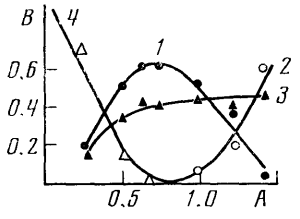

Figure 10. Relative amounts of the components of the hydride mixture in aluminium chloride-ether; A—molar component ratio $LiH : AlCl_3$; mole fraction B (not including the ether): 1) of $AlHCl_2.AlCl_3.(C_2H_5)_2O$.ether; 2) $AlH_2Cl.AlCl_3.(C_2H_5)_2O$.ether; 3) $LiAlCl_4$; 4) $AlCl_3.(C_2H_5)_2O$.ether.

According to the studies of Arkhipov and Mikheeva[47] and Kohler[75], the following mechanism of the ionisation of the hydride mixture is most likely:

$$\begin{aligned} 2AlHCl_2 \cdot AlH_2Cl \cdot ether &\rightarrow Al_2Cl_5 \cdot ether^+ + AlH_4^- \\ Al_2Cl_5 \cdot ether^+ &\rightarrow AlCl_2 \cdot ether^+ + AlCl_3 \cdot ether \\ &\quad \downarrow +AlCl_3 \cdot ether \\ &\quad AlCl_2^+ \cdot ether + AlCl_4^-. \end{aligned} \quad (5)$$

Anions of the AlH_4^- type are oxidised at insoluble anodes[76] and there is no direct involvement of the hydride mixture in the cathodic process. The potentials corresponding to the deposition of aluminium in ethereal hydride electrolytes and in an ethereal solution of aluminium chloride differ on average by 1–1.5 V, but, on smooth increase (decrease) of the hydride mixture concentration, the limiting current densities with respect to hydride ions are not observed at all (Fig. 11), regardless of the nature of the cathode. The electrodeposition is accompanied by the simultaneous liberation of hydrogen, which has no direct bearing on the current yield of aluminium, the latter being always 100%. This side effect can be accounted for by the

spontaneous decomposition (which is in general slight) of the alane complexes arising under the catalytic influence of the freshly formed surface of the aluminium deposit [78-80].

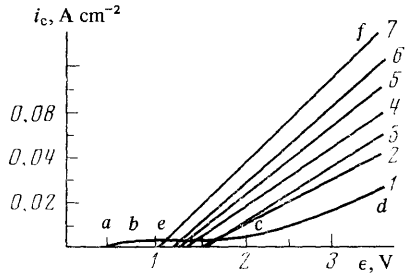

Figure 11. Variation of the cathodic polarisation of an aluminium electrode with increasing content of the hydride mixture in an etherate medium (2 M aluminium chloride, initial volume of electrolyte 30 ml); volume of added hydride mixture (ml): 1) 0; 2) 1; 3) 3; 4) 6; 5) 9; 6) 12; 7) 15; scan—0.8 V min^{-1}; reference electrode—Al(Ag). [77]

The nature of the complex cations of the etherate responsible for the electrodeposition of aluminium and ionisation mechanisms of types (1) and (2) for ethereal hydride electrolytes are to some extent confirmed also by the characteristics of the transport process (electrolyser with a glass membrane, aluminium anode).

Table 4. The transport of ether in the Lovet ethereal hydride electrolyte (i_c = 0.02 A cm^{-2}; volume of electrolyte 50 ml).

t, °C	V_{free}, ml*		V_{int}		Al deposit on cathode		N
	cathode (Cu)	anode (Al)	ml	mole	g	g-atom	
70	3.8	2.2	1.6	0.01533	0.1788	0.00666	2.3
80	3.7	2.7	1.0	0.00958	0.1126	0.00417	2.3
80	4.2	3.0	1.2	0.01150	0.1350	0.00500	2.3

* V_{free} is the volume of free ether collected from the electrode surface and V_{int} is the volume from the inner sphere of the cations.

When an anolyte with labelled chlorine ($H^{36}Cl$) and a non-radioactive catholyte are used at the beginning of electrolysis, the subsequent distribution of radioactivity in the working ethereal hydride bath makes it possible to establish the relation between the diffusion and migration of ions. The migration of $AlCl_4^{*-}$ to the anolyte under the influence of the current in the absence of the Cl^- ligand in the complex cation [81] should in all cases inhibit the diffusional equalisation of the radioactivities of the catholyte and anolyte over a period of time. On the other hand, in the presence of the Cl^- ligand, the effect of the current is varied. According to the Hittorf calculation, in a medium with an equal or greater mobility of $AlCl_4^-$ relative to that of the cation the transport of Cl^{*-} anions to the catholyte is inhibited by migration and for a higher mobility of $AlCl_2.ether^+$ the transport of Cl^{*-} (and hence the equalisation of the radioactivities in the course of time) is accelerated. The acceleration of the equalisation of radioactivities by current in the NBS ethereal hydride electrolyte is observed when the molar ratio A is reduced to values of the order of 0.1–0.2 (Fig. 12). There is apparently an appreciable simultaneous increase in the mobility of the $Al_2.ether^+$ cation.

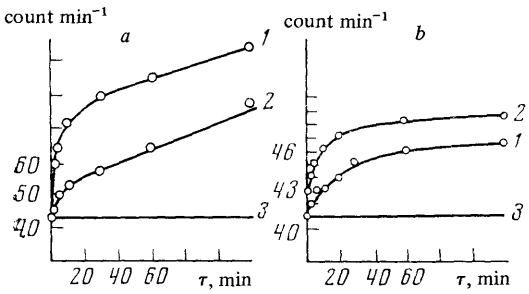

Figure 12. Increase of the radioactivity of the catholyte: *a*) A = LiH : $AlCl_3$ = 0.8; *b*) A = 0.2; 1) diffusion through a membrane (in the absence of a current); 2) superposition of migration (electrolysis); 3) supporting electrolyte; I = 40 mA; electrolyte volume 50 ml.

It follows from mechanisms (1) and (2) that the cation of the etherate is more solvated than the anion with a blocked aluminium atom. Furthermore, at the instant of the reduction of the cation the ether passes from the inner sphere to the free state. The distillation and trapping (by liquid nitrogen traps) of the ether at the instant of the reduction of the cations and the oxidation of the anions of the etherate on the electrode surface are most effective in the Lovet ethereal hydride electrolyte.

The absence of free ether in the Lovet electrolyte makes it possible to determine clearly the difference between the volumes of the ether trapped from the cathode and anode (Table 4). Since the current yield of aluminium at the cathode is 100% regardless of i_c, the ratio of this difference (in moles) to the number of gram-atoms of the aluminium deposit N expresses the number of ether molecules entering into the inner sphere of the cation as the second ligand. The value obtained N = 2.3 is somewhat too high owing to the impossibility of allowing exactly and separately for the total number of ether molecules constituting the solvation shells of the cation and anion, but, according to the results of a study of the transport process, the most probable composition of the cation is undoubtedly $AlCl_2.2(C_2H_5)_2O^+$. The result of the calculation agrees fully with the thermochemical and structural characteristics of aluminium chloride-ether.

In the remaining ethereal electrolytes (ethereal amine [39], ethereal ammonia [40], and ethereal dative [38] electrolytes) the ingredient which binds the solvated protons exhibits a marked chemical individuality. Such ingredients are either organic bases (in ethereal amine and ethereal dative electrolytes; their approximate composition is 1–3 M aluminium chloride or bromide, 5–20 mole% of the base relative to the etherate, and diethyl ether) or ammonia (in the ethereal ammonia electrolyte with the

composition 1–4 M aluminium chloride, 17–30 mole % of ammonia, and diethyl ether) which vigorously bind the protons of the ionised Wiberg-Brown complex[82-84] H. .ether$^+$.AlX_4^-—the product of the interaction of hydrogen halide with the complex cation of aluminium halide–ether. The reaction reduces to the formation of the stable AlX_4^- structure and protons weakly solvated by ether. Therefore the Wiberg-Brown complex is always present in preparations of an ethereal solution of aluminium chloride or bromide.

The distribution of the organic base (and ammonia) in the ethereal electrolyte as a whole is regulated by the equilibria

$$H.ether^+ + base = H.base^+ + ether, \quad (6)$$

$$AlX_3.ether + base = AlX_3.base + ether. \quad (7)$$

In view of the considerable excess of free ether, the low solubility of the type AlX_3.base complexes in the ethereal medium (according to analytical and spectrophotometric data and the results of studies of the electrolytic properties of the systems under consideration), equilibrium (7) is to a large extent displaced to the left[85-88]. Consequently the base is bound by the ethereal aluminium halide solution mainly as a result of the rightward shift of equilibrium (6). This is indicated by the distinct decrease of i_{lim} for the H.ether$^+$ ions (Fig. 13) following the addition of the base. The converging series of values of i_{lim} reflects the existence of equilibrium (6) and its rightward shift.

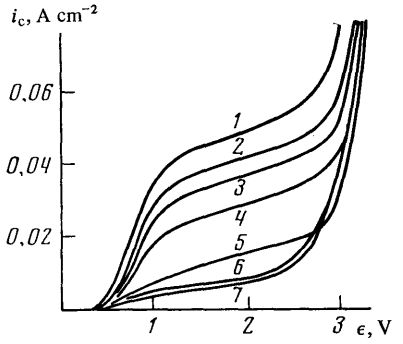

Figure 13. Effect of added base in an ethereal solution of aluminium chloride on i_{lim} for the solvated protons H.ether$^+$; amount of base (hexamethyleneimine, mole %): 1) 0.00; 2) 0.25; 3) 1.00; 4) 1.60; 5) 2.40; 6) 4.00; 7) 6.10.

The Lewis acidity in relation to protons in the bulk of the ethereal electrolyte and in the diffusion layer of the cathode under the conditions of a current can be expressed by the residual concentration of the free H.ether$^+$ ions. The optimum conditions for the electrocrystallisation of aluminium arise only in the absence or at a vanishingly low concentration of the H.ether$^+$ ions, i.e. for a high Lewis basicity of the medium. Otherwise the process is complicated by the presence of the electroorganic component, catalysed by the solvated H.ether$^+$ protons in the presence of free ether molecules (a dark dispersed powder is deposited on the cathode). Etherate electrolytes in which there is no free ether at all constitute an exception. Therefore in etherate electrolytes H.ether$^+$ ions do not exhibit a catalytic activity and a high quality crystalline aluminium deposit is obtained in the presence of even large concentrations of the Wiberg–Brown complexes[89]. A high basicity is always readily generated in ethereal hydride electrolytes owing to the decomposition of the Wiberg–Brown complex by the compounds constituting the hydride mixture [a complete rightward shift of equilibrium (6)][51,79].

The remaining electrolytes [with an incomplete rightward shift of equilibrium (6)] are distinguished by a more complex mechanism for the attainment of a high Lewis basicity. A high quality deposit arises on the cathode only after a preliminary passage of a current (4.0–4.8 Ah per litre of solution), i.e. after an additional decrease of the residual concentration of the H.ether$^+$ ions owing to the electrolytic liberation of hydrogen. In consequence of the low rate of interaction of the complex H.base$^+$ and ether, a steady-state distribution of the components of equilibrium (6), close to the distribution which obtains when the equilibrium is completely displaced to the right, arises under the influence of the current.

When a current is passed through ethereal electrolytes, there are a number of features which reflect directly the changes in electrocrystallisation conditions. The values of i_{lim} for H.ether$^+$ ions on the cathodic polarisation curves fall to zero only as a result of the current (Fig. 14); curve 4 in the same Figure reflects the variation of i with ϵ under the optimal electrodeposition conditions.

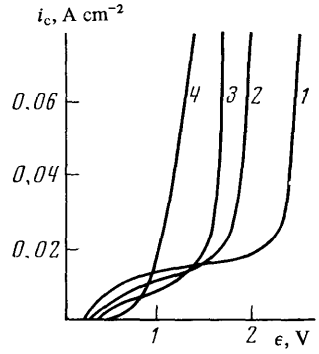

Figure 14. Variation of cathodic polarisation during the passage of a current through the ethereal electrolyte (base—hexamethyleneimine): 1)–3) decrease of the residual concentration of H.ether$^+$ ions (dispersed deposit); 4) electrodeposition under the conditions of high basicity (dense crystalline deposit); galvanostatic conditions; reference electrode—Al(Ag).

The increase of basicity on passage of a current can be expressed quantitatively as an increase of conductivity (Fig. 15) or as a negative shift of the platinum probe potential reversible with respect to H.ether$^+$. The considerable decrease in conductivity can be explained by the weakness of the H$^+$–ether bond ($pK_a = -3.59$) relative to the H$^+$–base bond ($pK_a = 7.3–12.3$)[38]. The reversibility of the probe electrode potential relative to H.ether$^+$ is a result of the saturation of the electrolyte by cathodic hydrogen.

In the presence of Lewis bases and ammonia, potentials of the probe cell in the range between −0.3 and −0.6 V (the probe potential is negative) correspond to optimal electrocrystallisation (a dense crystalline deposit). In the absence of bases (a dispersed deposit is formed regardless of the amount of electricity passed through the system) the potential is limited to 0.0–0.2 V (the probe potential is positive). In ethereal hydride electrolytes the very presence of the hydride mixture alters the cell potential to between −0.9 and −1.1 V, as a result of which the necessity for exposure to a current is eliminated.

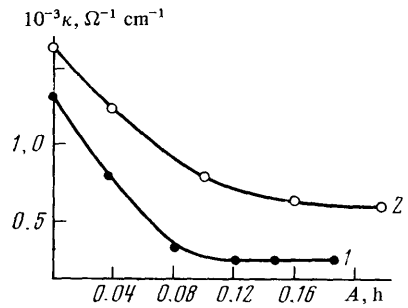

Figure 15. Variation of the conductivity of the ethereal electrolyte during the passage of a current: 1) base—piperidine; 2) base—hexamethyleneimine.

The elimination of the electroorganic component of the electrodeposition process (transition from a dispersed deposit to a dense crystalline deposit) in general increases the purity of the coating. However, under optimal electrocrystallisation conditions in ethereal ammonia and ethereal dative electrolytes, side processes persist at elevated current densities ($i_C > 0.005$–0.010 A cm^{-2}): there is a weak evolution of hydrogen owing to equilibrium (6) and possibly an additional electroorganic reaction. For this reason, in the given group of electrolytes the current yield of aluminium in certain cases does not exceed 75–80% following an increase of i_C and the morphology of the deposit may be complicated by local spheroidal formations[90–92].

The significant characteristics of electrode polarisation in ethereal electrolytes are high exchange current densities [$(2.0–5.0) \times 10^{-4}$ A cm^{-2} in etherate electrolytes and 1.6×10^{-3}–4.3×10^{-4} A cm^{-2} in ethereal hydride electrolytes] and high temperature coefficients of the overvoltage (which usually exceed by an order of magnitude the analogous values in an aqueous medium) 0.01–0.03 V deg^{-1}, as a result of which the kinetics of the reduction of the etherate cations when $i_C < 0.01$ A cm^{-2} depend on the superposition of limitations due to the reaction (in etherate electrolytes), crystallisation, and diffusion (in the NBS ethereal hydride electrolyte; in this case the Faraday impedance can be represented by the equivalent circuits for the transition, diffusion, and crystallisation–see Fig. 16). In the range $i_C = 0.10$–0.40 A cm^{-2} diffusion-dependent limitations fully predominate (ethereal hydride and ethereal ammonia electrolytes). Since free dilution of the etherate phase by ether is ruled out, the properties of the limiting current density of the diffusion overvoltage (the dependence of i_{lim} on the molarity of the etherate, the content of the hydride mixture and organic bases, temperature, rate of stirring, etc.) can be investigated exclusively by a pulse technique. The transition time for strong current pulses can be determined only when a rigorous correspondence between the true and induced currents i_C is maintained (< 0.40 A cm^{-2}). For this purpose, the treatment of the test electrode must ensure the homogeneity of the surface and inhibition of the growth of crystal nuclei during the pulse (galvanostatic switching on)[51,71,80,90,93].

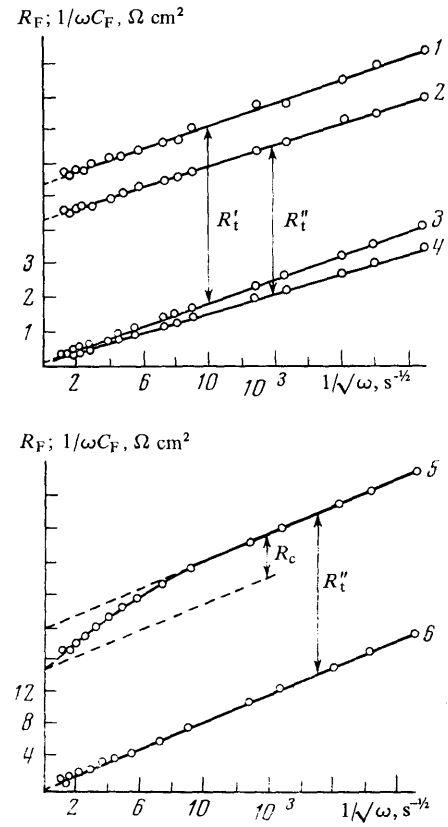

Figure 16. Components of the Faraday impedance; aluminium electrode: 1) R_F; 3) $1/\omega C_F$; Al(Hg) electrode: 2) R_F; 4) $1/\omega C_F$; Al(Hg) electrode: 5) R_F; 6) $1/\omega C_F$; measurements in aluminium bromide–ether.

V. THE OVERVOLTAGE OF HYDRIDE HYDROGEN

The behaviour of soluble and insoluble anodes in all ethereal electrolytes is determined by the oxidation of the AlX_4^- anions from the etherate with the exception of hydride media where the anodic process is complicated by the involvement of the AlH_4^- ($Al_2H_7^-$) ions[75,76,80,81]. In the case of an insoluble electrode AlH_4^- ions are oxidised under conditions corresponding to the first section of the anodic polarisation curve ($i_C \leq 0.01$ A cm^{-2}, $\epsilon \leq 1.5$ V). Consequently the above ranges of the i_C and ϵ values are convenient for the measurement of the overvoltage of hydride hydrogen.

The concept of electrolytic desorption proposed by Heyrovsky is justified by the nature of the protons $H.aq^+$ solvated by water. Hence the hypothesis that the potentials of the spent and anodically polarised electrode in the ethereal hydride electrolyte depend on the Volmer–Tafel mechanism is quite natural. After replacing $H.aq^+$ by $H.hydr.^-$, the mechanism becomes

$$\begin{aligned} H^- &\rightleftharpoons H + e, \\ H + H &= H_2. \end{aligned} \qquad (8)$$

Thus examination of the hydride hydrogen overvoltage could also permit the solution of the problem of the relation between the successive discharge and recombination stages. Calculation of the overvoltage from the Tafel relations or the equations of the Kheifets pulse technique leads to large numerical values of the exchange current density (Table 5) and the coefficient b and to extremely small transition coefficients α (Table 6).

Table 5. The exchange current densities at the hydride hydrogen overvoltage ($-\lg i_0^*$).

Electrode	Temperature, °C				Electrode	Temperature, °C			
	10–12	15–18	24–25	30		10–12	15–18	24–25	30
Ag	3.4	3.2	2.9	2.8	Sn	—	3.6	2.8	2.5
Ni	—	6.0	5.8	5.7	Pb	5.0	4.5	—	3.2
Zn	—	4.5	3.5	3.2	Pt	5.5	5.3	5.0	4.7

Table 6. The coefficients b and α for hydride hydrogen (t = 20°C).

Electrode	b, V	α	Electrode	b, V	α	Electrode	b, V	α
Ag	0.56	0.105	Zn	0.28	0.210	Pb	0.22	0.267
Ni	0.55	0.107	Sn	0.39	0.150	Pt	0.38	0.155

Table 7. A series of Tafel coefficients a at the hydride hydrogen overvoltage.

Electrode	a, V	Electrode	a, V	Electrode	a, V
Pb	0.9	Sn	1.3	Pt	2.0
Zn	1.1	Ag	1.7	Ni	3.4

In terms of the values of b, the Tafel relations for hydride hydrogen express the overvoltage of the transition, i.e. the kinetics of the oxidation of the AlH_4^- ($Al_2H_7^-$) ions are determined by the discharge reaction and not the recombination reaction. Furthermore, the possible influence of the spontaneous decomposition reactions of the hydride mixture on the oxidation of hydride hydrogen reduces the probability of a mixed mechanism for overvoltage of the type under consideration.

The low values of the coefficient α indicate a high activation energy for the reverse Volmer reaction [Eqn. (8)], which is equivalent to hindrance characteristic of the formation of structures deformed by hydride hydrogen. For the hydride hydrogen overvoltage, the sequence of the activation energies for the forward Volmer reaction differs appreciably from the classical sequence, usually represented by a series of increasing Tafel coefficients a (Table 7)[94,95].

VI. INDUSTRIAL APPLICATIONS OF ETHEREAL ELECTROLYTES

The aluminium deposits coating the surfaces of various metals at room temperature in ethereal electrolytes are obtained in the form of dense, homogeneous plate of high purity[8,11,16,18,26,50]. The usual technical procedures (stirring, adjustment of the position of the rods, regulation of the electrolyte stream, periodic filtration, employment of certain additives) make it possible to vary the thickness of such coatings from several micrometers to 2–3 mm, while ensuring at the same time the necessary uniformity. The advantages of electrolytic aluminium (small weight, high thermal conductivity, electrical conductivity, and reflectivity, effective anticorrosion properties, low melting point, only slight deterioration in the properties of the coated metal under the conditions of heat treatment, and low cost) compared with zinc, tin, cadmium, gold, and titanium–silver coatings have greatly increased interest in the aluminium-plating process in ethereal electrolytes in the field of both modern electroplating technique and in galvanoplastics. Mainly ethereal hydrides (NBS, Lovet, and Etmac) electrolytes have been recommended for electroplating baths in technological and industrial-technological processes.

The most important stages in electroplating processes are the choice of the surface to be coated (usually steel, copper, nickel, Kovar, titanium, and silicon), the search for a technique to be used in the preparation of the surface for aluminium plating giving a reliable adhesion of the coating, and the design of a hermetically sealed bath and electrode rods (in an atmosphere of dry nitrogen or argon). Various workers have often used the so called aliphatic acid treatment of the surface, originally proposed by Schickner[96,97]. Before being immersed in the ethereal hydride bath, the metal surface is uniformly coated by a crystalline layer of aliphatic acid (oleic, linolenic, etc.) or by a layer of salicylic, benzoic, pyrogallic, phenylacetic, or heptafluorobutyric acid[11]. The onset of the aluminium electrodeposition process (the switching on of the working current) is synchronised with the dissolution of the layer of acid in the electrolyte. The aliphatic acid treatment requires expensive reagents and must be performed with exceptional precision. The maximum adhesion of the coatings is achieved by selecting the appropriate acid and the appropriate duration of the individual operations in the treatment in relation to various aluminium-plated metals. An easier and universal method of preparing the surface for aluminium plating involves chemical or anodic etching of iron, steel, Kovar, nickel, and copper in hydrochloric acid[53,75], phosphate, nitric acid, and hydrogen peroxide[98–100] solutions, which prevent saturation with hydrogen.

Industrial-technological aluminium plating of constructional titanium rods (NBS ethereal hydride electrolytes) was achieved by Hess and Betz[101]. Aluminium plating at room temperature is hardly reflected in the mechanical properties of the rods. An appreciable corrosion resistance of the components was achieved. The authors note that different variants of their technology

can be used for the aluminium plating of titanium components of more complex shape, certain parts of laboratory and workshop furniture, and also individual units in microelectronics (including, for example, the local aluminium plating of locating frames).

Electroforming techniques for aluminium have found extensive applications (NBS, Lovet, and Etmac ethereal hydride electrolytes). Buschow and Esola[102] and Schmidt and Hess[103] developed a process and designed a manufacturing set up for the construction of high-quality light aluminium reflectors for the concentration of solar energy (18 and 76 cm in diameter). Aluminium layers are grown at room temperature on nickel and silver templets with mirror-bright surfaces. The improvement in the design of the ethereal hydride bath hermetically sealed under argon and nitrogen is noteworthy; the authors increased the volume of the bath to 700–800 litres. The construction of aluminium reflectors was developed in processes used in the manufacture of telescopic reflectors, non-magnetic optical systems, light and precision mirrors, and optical systems for cosmic space apparatus.

Another trend in the development of techniques for electrolytic aluminium plating using ethereal electrolytes involves the electroforming of layers with fillers. The technique of the preparation of matrix composites (with boron rods, silicon carbide, beryllium, steel, and graphite fibres as fillers), which are light, very hard, and at the same time elastic, to be used in the construction of components of cosmic space apparatus, has been proposed and successfully introduced by Hanson et al.[104] and Withers and Abrams[105]. Electroforming techniques for aluminium have considerable advantages over other methods for the preparation of matrix composites, since electrodeposition in the range of room temperatures hardly influences the properties of the fillers themselves, which makes it possible to increase sharply the set of physicomechanical properties of the composites themselves and at the same time achieve an exceptionally high strength to weight ratio for such composites.

A new stimulus to further improvement of the manufacture of solar batteries arose from the technology of the deposition of aluminium layers (NBS ethereal hydride electrolyte) on the surface of silicon sections proposed by Lui and Yasui[106]. Aluminium terminals simplify the construction and parallel connection of aluminium sections compared with the earlier technology in which a titanium–silver alloy was used.

Manufacturing–technological processes involving the electrodeposition of aluminium from ethereal electrolytes at room temperature have greatly increased practical and theoretical interest in this field of electrochemistry.

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Reactions of Oxo-derivatives of Furan with Hydrogen Peroxide and Peroxy-acids

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The reactions of furan oxo-compounds with hydrogen peroxide and with peroxy-acids are surveyed, different views on the reaction mechanism are discussed, and modern concepts are explained. Possible practical applications of the process are shown. Comparison with the oxidation of aromatic compounds under similar conditions indicates several specific features of the process in the furan series. The bibliography contains 160 items.

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I. INTRODUCTION

The oxidation of oxo-derivatives of furan by hydrogen peroxide and peroxy-acids yields such valuable products as furancarboxylic, oxo, and dibasic acids, lactones [1-14], peroxides of carbonyl compounds of the furan series, furyl formate, its homologues, and derivatives, and also unsaturated lactones [6,8,15-18]. However, by no means all potentialities of this process have been realised. The reaction is extremely sensitive to the nature of the solvent used, the temperature, and the proportions, concentration, and structure of the reactants. This enables its direction to be controlled, and provides ready methods for obtaining new compounds [8,17,18].

II. DEVELOPMENT OF IDEAS ON THE REACTION OF FURAN OXO-COMPOUNDS WITH HYDROGEN PEROXIDE AND PEROXY-ACIDS

The prospect of utilising the reactions of furan oxo-compounds with hydrogen peroxide has been established only during recent decades. For a long time investigators were unable to isolate any products other than maleic and succinic acids [3,7,9,19-23] because of the absence of systematic work, although these acids are formed as a result of fundamental changes in more valuable oxo-acids and lactones [4,5].

The reaction of 2-furaldehyde with 3% hydrogen peroxide in the presence of iron(II) sulphate was first accomplished in 1899 by Cross et al. [19], who postulated the formation of hydroxo-2-furaldehyde and hydroxyfuran-2-carboxylic acid. Neither they nor subsequent investigators were able to isolate these products, and later an error in identifying the latter was demonstrated. The mechanism of the reaction was not considered. Succinic, maleic, and fumaric acids have since been isolated (in 20-50%, 10-40%, and 2-25% yields respectively) from the oxidation of 2-furaldehyde by hydrogen peroxide in water [1,3,9,20-23]. Several workers have reported the formation of formylacrylic acid, either detected qualitatively or isolated as the unpurified product in yields up to 25%. [1,23] Formic acid was formed in all cases. Pyromucic acid could be obtained only when furaldehyde was oxidised with hydrogen peroxide in pyridine [2,24].

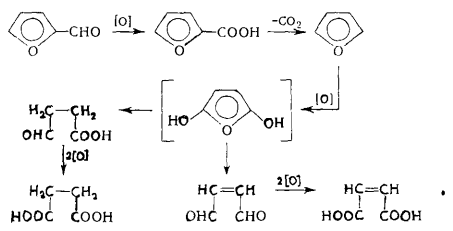
Very little information is available on the oxidation of furan oxo-compounds by peroxy-acids. The action of Caro's acid on 2-furaldehyde yields succinic and formic acids [25]. Oxidation by aliphatic and aromatic peroxy-acids gives a mixture of maleic, formic, formylacrylic, and succinic acids in proportions varying with the conditions [7,26,27]. Hydroxy-lactones may also be formed [26]. Marked resinification accompanies oxidation by peroxy-acids. In isolated cases succinic acid is not detected when 2-furaldehyde is oxidised by peracetic acid, but only formylacrylic, maleic, and fumaric acids [28]. A similar result has been obtained in the oxidation of 2-acetylfuran. A mixture of γ-oxovaleric and 4-oxopent-2-enoic acids is formed by the oxidation of 5-methylfuran-2-al by peracetic acid [28]. Furancarboxylic acids were not found among the oxidation products from carbonyl derivatives with peroxy-acids, but aldehydes gave the theoretical yield of formic acid, and ketones similarly formed acetic acid.

Some authors consider that the initial attack by hydrogen peroxide on 2-furaldehyde takes place at the furan ring [1,19,29], and others at the aldehyde group [22,23]. Salchinkin [22] supposes that the oxidant is active oxygen formed from hydrogen peroxide, which oxidises the furaldehyde at the carbonyl group to pyromucic acid, and the latter then undergoes decarboxylation to furan. Conversion of this product into the hypothetical furandiol is followed by the formation of malealdehyde and succinaldehyde, and finally maleic and succinic acids (Scheme 1). Only these acids were isolated among the products included in Scheme 1. No other evidence was given.

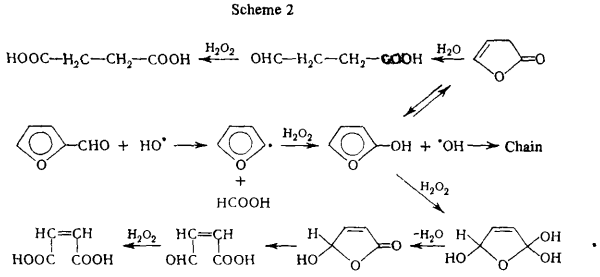
An alternative mechanism also involving the carbonyl group as the reactive centre entails oxidation by the hydroxyl radical (Scheme 2) [23]. Pyatnitskii and Lapkova suppose [23] that the reaction passes by a homolytic chain

mechanism through furanol and its tautomeric form (crotonolactone), which are converted into the β-formyl acids and then oxidised to maleic and succinic acids. The only evidence given in support of this scheme comprises isolation of the dibasic acids and the qualitative detection of 4-oxobut-2-enoic acid.

Scheme 1

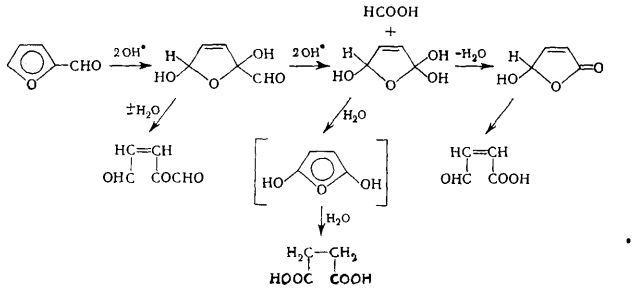


Scheme 2



Clauson-Kaas and Fakstorp[29] regard the interaction of 2-furaldehyde with hydrogen peroxide in alcoholic solution containing added osmium tetroxide as starting at the diene system of the furan ring, without indicating whether the mechanism is homolytic or heterolytic (Scheme 3). The mechanism suggested by Kallay[1] differs only in preliminary protonation of the heterocycle at the oxygen atom followed by ring opening and subsequent cyclisation. This assumes that the radical reactions of hydroxylation of the ring are coupled with the ionic reactions of its opening.

Scheme 3



No detailed consideration has been given to the mechanism of the oxidation of furaldehyde by peroxy-acids. It was suggested[26] that opening of the furan ring begins with formation of an unstable oxide involving one of the double bonds, while formic acid is obtained as a result of detachment of the aldehyde group; no information was given on the structure of the oxide or the mechanism of the process.

No proofs were given of the reliability of the mechanisms suggested for the oxidation of furaldehyde by hydrogen peroxide and peroxy-acids. They are inconsistent with modern views on the reactions of carbonyl compounds with these reagents, and do not take into account the formation and transformation of organic peroxy-compounds[30-32]. Nor are the schemes consistent with available information on the structure and reactivity of furan oxo-compounds and hydrogen peroxide; the mechanism is not related to the structural features of the reactants or the reaction conditions.

Discussion of the mechanism of the reactions between furan oxo-compounds and hydrogen peroxide or peroxy-acids cannot be based on any close analogy with corresponding reactions of aliphatic and aromatic aldehydes: the structure and the properties of furan systems are so specific that special consideration must be given even to whether the peroxide attacks the carbonyl group or the ring.

III. STRUCTURAL PECULIARITIES AND REACTIVITY OF FURAN OXO-COMPOUNDS AND HYDROGEN PEROXIDE

The reactions of 2-furaldehyde are often divided into aldehydic, diene, and ethereal.

The series of compounds—furan, 2-furaldehyde, and benzaldehyde—differ significantly in structure and properties. Thus no analogy is observed in the diene properties of furan and furaldehyde. Furan reacts with active dienophiles, whereas furaldehyde and other derivatives containing electron-accepting substituents (pyromucic acid, nitrofuran, etc.) do not react at all as dienes[33-38]. Furaldehyde itself is able to act as a dienophile[39]. Products of addition at the diene system of furaldehyde could not be isolated from the reactions of it and its derivatives with molecular oxygen even with active initiation by light[40-42,59].

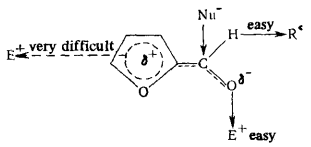
These facts are fully consistent with the view that oxygen adds only to those 1,3-dienes having enhanced electron density at the site of addition[43]. In furaldehyde, its homologues, and isomeric ketones the furan ring is conjugated with the carbonyl group, with displacement of electron density towards the latter. This is indicated by numerous data on the dipole moments[44,45], ultraviolet[6,46], infrared[6,47,48], proton magnetic resonance[48-50], and Raman[51] spectra, as well as the molecular exaltation. The infrared spectra show that the carbonyl group in furaldehyde lies in the plane of the ring owing to conjugation with the latter. The vector of the dipole moment is directed towards the carbonyl group with $\mu = 3.61$ D. The degree of conjugation between the π-bonds of the furan ring and the carbonyl group is clearly demonstrated by a comparison of the ultraviolet spectra of 2-furaldehyde and fur-2′-ylacetaldehyde, in which the carbonyl group is not conjugated with the ring ($\lambda_{max} = 277$ and 220 nm respectively). Calculation of the π-electron density shows considerable diminution in the ring and enhancement on the carbonyl oxygen in furaldehyde[52,53]. These facts are evidence of marked impoverishment of the electron density of the heterocycle and enrichment of the π-bond of the carbonyl group. This in turn strengthens the participation of p-electrons of the oxygen heteroatom in conjugation with the π-electrons of the ring. Hence the furan ring is more strongly aromatic in furaldehyde than in furan itself. This feature of the electronic structure of the furaldehyde molecule eliminates reactions involving the cyclic diene bonds, even with hydrogen peroxide. Thus Scheme 3 and

similar mechanisms[1,29] are inconsistent with modern views on the structure and properties of 2-furaldehyde.

Protolytic or hydrolytic cleavage of the furan ring by rupture of the C–O–C bond may be expected in systems containing hydrogen peroxide and especially its aqueous solutions. With regard to the acidophobic nature of furan compounds it is supposed that the cyclic oxygen atom forms a dative bond with the proton (oxonium ion) by means of the lone pair of electrons not involved in conjugation, which breaks down, and the ring is cleaved[54-56]. On the other hand, a vast amount of experimental work has been published indicating that electrophilic reagents do not attack the heteroatom but a cyclic carbon atom to form α-substituted furan derivatives[57]. The electron density on the cyclic oxygen atom is already low in the furan molecule, still lower in furaldehyde[52,53], and interaction with a proton cannot be ensured. The protonation of aromatic ethers involves the disruption of $p-\pi$ conjugation (E_{conj} = 8–12 kcal mole^{-1}), and occurs only if the energy of the resulting dative bond exceeds the conjugation energy[58]. Oxonisation is difficult with diphenyl ether, and is impossible at the heterocyclic oxygen atom in furaldehyde: this oxygen already possesses an oxonium character, and the energy of conjugation is very high.

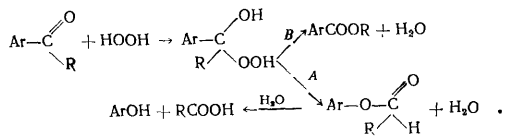
It has been proved experimentally that furaldehyde undergoes protonation not at the cyclic oxygen atom but throughout the conjugated system with formation of π-complexes[59,60]. This is consistent with the supposed π-functionality of the furan ring in complex formation[61]. In furaldehyde the end of the conjugated system having enhanced electron density is the aldehydic oxygen atom, to which a proton attaches in the limiting case. The protonation of furaldehyde by acids is accompanied by a strong bathochromic shift of the ultraviolet bands. Experiments suggest that electrophilic, nucleophilic, and radical reactions involve predominantly the aldehyde function, owing to the distribution of electron density in furaldehyde. Reaction will be favoured energetically if a stable transition state is established, in which the conjugation of the ring is preserved. The aldehydic carbon–hydrogen bond is less stable than a similar bond in the furan ring (70 and 103 kcal mole^{-1} respectively). Thus the direction of reactions in furaldehyde can be represented by Scheme 4, where R· is a free radical, E^+ an electrophilic species, and Nu^- a nucleophilic species. This scheme has been confirmed experimentally in the reduction[62] and the acetalation[63] of furan oxo-compounds. There are no grounds for supposing that reactions with hydrogen peroxide and with peroxy-acids will constitute exceptions.

Scheme 4



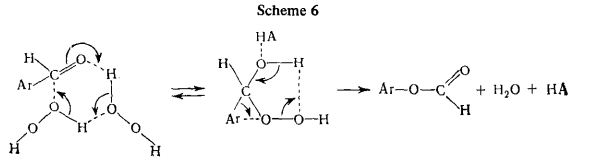
It does not follow that the reaction of furan oxo-compounds with these reagents will be analogous to that of the corresponding benzene derivatives, which also begins at the carbonyl group. Furaldehyde is more polar and more easily polarised than is benzaldehyde, as shown by the higher dipole moment and dielectric constant of the former. Experiment suggests that the π-electron system of the furan ring is more mobile than that of the benzene ring[44,46,64], which can be attributed to the presence of two oxygen atoms: the heterocyclic oxygen is a donor, and the carbonyl oxygen an acceptor, of electrons. As a result, the electron density and also the basicity of the ring are lower, while those of the carbonyl group are higher, than in benzaldehyde. On the other hand, furyl is more electronegative than is phenyl: the dissociation constant of pyromucic acid is 76.2×10^{-5}, tenfold that of benzoic acid (6.3×10^{-5}), which can be attributed to the weak aromaticity of furyl and its definite unsaturation. A significant difference in reactivity towards hydrogen peroxide and peroxy-acids should be observed between oxo-compounds derived from furan and benzene respectively. On the other hand, there are no grounds for supposing that these differences will be apparent in the direction of the early stages of interaction with the carbonyl group: only differences in reaction velocity are to be expected here.

Scheme 5



The oxidation of oxo-derivatives of benzene by hydrogen peroxide can be represented[30-32,65-69] by Scheme 5: hydrogen peroxide adds at the carbonyl group to give a hydroxy-hydroperoxide[67,69], whose formation in the aromatic and aliphatic series has been demonstrated by isolation or spectroscopically[70-73]. The resulting peroxide undergoes an intramolecular Baeyer–Villiger rearrangement[74], which is substantially accelerated by acids. In the case of benzaldehyde the rearrangement leads either to an ester (hydroxyphenyl formate) or to benzoic acid. Rearrangements of this type are widespread. Discussion of the mechanism of the formation and rearrangement of peroxides in the oxidation of aromatic and aliphatic oxo-compounds by hydrogen peroxide and peroxy-acids has considered as intermediate stages heterolysis[30,66,67,75-78], homolysis[79-81], or activated complexes[67,75-78]. A mechanism involving the molecular formation and rearrangement of hydroxy-hydroperoxides has the most convincing theoretical and experimental support[31,82-84]. Reactions of this type (Scheme 6) involve a continuous transition from the initial to the final state without formation of kinetically independent ions or radicals. This is due to the wave properties of electrons, the high polarity and the polarisability of bonds in oxo-compounds and peroxides, and the far greater instability of activated bonds in transition complexes in comparison with ordinary bonds[85-91].

Scheme 6



Transition states are usually regarded as stable five- or six-membered cyclic complexes [31]. An important part in these processes is played by acids, which largely polarise carbonyl and peroxide bonds, thereby promoting the formation and transformation of the transition complexes [31]. Arguments in support of molecular mechanisms do not exclude the probability of complete ionisation, adequate reasons for which have been given for the stage of peroxide formation [75], and this probability is increased by the effect of strong acids and bases.

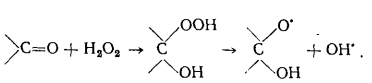
Irrespective of whether the hydroxy-hydroperoxide undergoes rearrangement by an ionic or by a molecular mechanism, it involves migration of one of the groups (Ar or R in Scheme 5) to the peroxide oxygen atom of diminished electron density. Migration of a hydrogen atom or the group R yields benzoic acid or its ester (Scheme 5*B*); that of aryl residues yields phenyl esters (Scheme 5*A*), which are then hydrolysed to phenols and acids. The relative migratory power of the groups varies in the sequence [30,68]

$$HOC_6H_4 > MeC_6H_4 > H > Ph > ClC_6H_4 > NO_2C_6H_4 > Me\ .$$

Similar data are not available for furan derivatives.

The main product of the oxidation of benzaldehyde is benzoic acid, in conformity with the greater ease of displacement of hydrogen than of phenyl. The simultaneous formation of small quantities of phenol and formic acid indicates the significance of the migration of phenyl. Electron-accepting substituents strongly impede such migration, and oxidation goes solely towards formation of benzoic acids. Electron donors, on the other hand, facilitate the formation of phenyl formates, and oxidation occurs very readily [30]. These results, as well as investigations using an oxygen isotope [92], have shown the untenability of the mechanism [93] of direct hydroxylation of the benzene ring by hydroxyl radicals. In the oxidation of salicylaldehyde by hydrogen peroxide the carbonyl group is the reactive centre, and a molecular activated complex is formed in which the *o*-phenoxy-group can easily migrate to an oxygen atom. As a result, the main oxidation product is catechol [92], whereas 3,5-di-t-butylbenzaldehyde yields the corresponding dialkylphenol and formic acid [94].

It is quite important to discuss the possible modes of breakdown of hydrogen peroxide in considering the mechanism of the oxidation of oxo-compounds. Some authors suppose that oxidation is effected by the cation HO^+ formed from hydrogen peroxide [95,96], but this is not supported by isotopic investigations [97–100]. The existence of an independent species HO^+ is improbable [101]. According to Denisov [102] ketones promote the homolysis of hydrogen peroxide:



It has been suggested [103] that radicals are formed in oxidations catalysed by certain strong acids in anhydrous medium:

$$H_2O_2 + H^+ \rightleftarrows H_3O_2^+ \xrightarrow{H_2O_2} H_3O^+ + HO^{\cdot} + HO_2^{\cdot}\ .$$

These processes are regarded as an exception to the general rule.

Oxo-compounds of low polarity in non-polar solvents, or in their absence under conditions of thermolysis, photolysis, or radical initiation, are able to react with hydrogen peroxide also by a homolytic mechanism [101]. In polar media (water, alcohols, organic acids, etc.), however, the mechanism is heterolytic [101,104]. Such a path is energetically more favourable, since solvation of the polar hydrogen peroxide molecule (μ = 2.13 D and ϵ = 73.1) [101,105] and its decomposition products greatly diminishes the energy of rupture of the bonds. Aqueous solutions of hydrogen peroxide have an acid reaction [101,105,106]:

$$H_2O_2 + H_2O \rightleftarrows H_3O^+ + HO_2^-.$$

Acid dissociation predominates over other types of breakdown [106] and increases with rise in temperature and increase in the hydrogen peroxide concentration of the solutions up to 80%. This compound also undergoes autoprotolysis:

$$H_2O_2 + H_2O_2 \rightleftarrows H_3O_2^+ + HO_2^-.$$

The degree of dissociation of hydrogen peroxide is determined by the nature of the solvent, the acidity of the medium, and the basicity of the substrate.

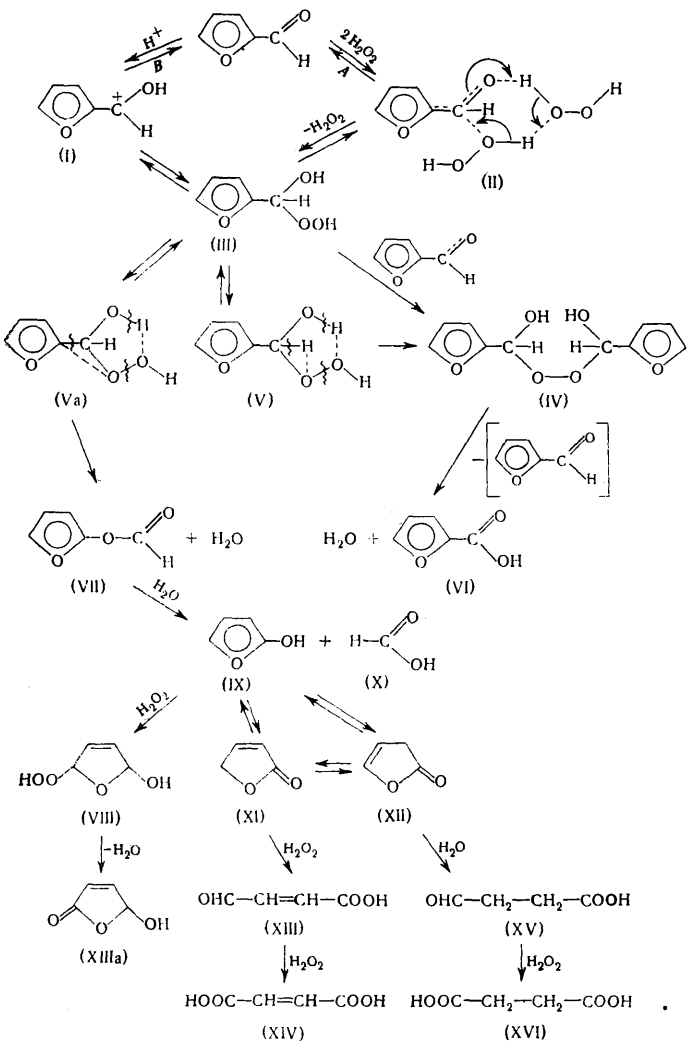
The high polarity and the polarisability of aromatic and especially furan oxo-compounds, their basicity due to the carbonyl group, the polar media used, and the relatively low temperatures—all these factors show that the reactions with hydrogen peroxide and peroxy-acids take place by a heterolytic or molecular mechanism. Either the hydrogen peroxide anion HOO^- or the molecule as a whole can act as nucleophilic reagent at the carbonyl group; it is also the proton donor.

Thus published experimental and theoretical results on the structure and properties of oxo-derivatives of furan and hydrogen peroxide, as well as the reactions of the latter and of peroxy-acids with aromatic oxo-compounds, show that Schemes 1–3 have no basis in fact. They and similar schemes cannot be used to describe the mechanism of the reactions of 2-furaldehyde and other furan oxo-compounds with these reagents. They are inconsistent with the structure and properties of furan aldehydes and ketones and of hydrogen peroxide, disregard the vast amount of experimental information on the peroxide oxidation of benzaldehyde and its derivatives, and do not provide for the formation of intermediate peroxy-compounds. Other concepts have therefore been advanced, and confirmed experimentally, to explain the mechanism of the oxidation of furan oxo-compounds by hydrogen peroxide and peroxy-acids.

IV. CURRENT IDEAS ON THE MECHANISM OF OXIDATION OF FURAN OXO-COMPOUNDS BY HYDROGEN PEROXIDE AND PEROXY-ACIDS

The special features of the reactivity of furan oxo-compounds and hydrogen peroxide and the reactions of aromatic carbonyl compounds with this reagent and peroxy-acids are taken into account in Scheme 7. The oxidation of the furan derivatives is regarded as a consecutive reaction having an ionic–molecular mechanism [4,5,120,126]. Here the carbonyl group is attacked initially either by a hydrogen peroxide molecule (reaction *A*) or by a proton (*B*). The predominance of *A* or *B* is determined by the structure of the carbonyl compound and by the reaction conditions. An intermediate linear or cyclic complex (II) is quite probably formed by reaction *A*, and the protonated species (I) by reaction *B*. The common result of the first stage is formation of the α-hydroxy-hydroperoxide (III), which may be converted, perhaps via the complex (V), either into the furyl ester (VII) or into the $\alpha\alpha'$-dihydroxy-peroxide (IV) depending on the structure and the reaction conditions. The corresponding furancarboxylic acid (VI) might be formed from (III) or

Scheme 7



from (IV). These stages show an analogy with the mechanism of the corresponding reactions in the benzene series (Scheme 5).

Significant differences in reaction velocity and proportions of products can be expected between furan and benzene derivatives, because of the greater mobility of the π-electron system of the furan ring. The rate of rearrangement of the peroxide (III) into the ester (VII) should be far greater with furaldehyde than with benzaldehyde. Furthermore, the rearrangement is stimulated in the furan series by hydrolysis of the ester to furanol (IX) and formic acid (X). The reverse reaction is improbable in this case, since the products of hydrolysis—(IX), (XI), and (XII)—are converted irreversibly into acids—4-oxobut-2-enoic (XIII), maleic (XIV), γ-oxobutyric (XV), and succinic (XVI). In the case of benzaldehyde, its derivatives, and its homologues, compounds containing stable aromatic rings are formed at all stages, and reactions involving cleavage of the ring are not observed (Scheme 5).

The oxidation of furan oxo-compounds is accompanied by substantial variation in the stability of the heterocyclic ring in the initial and intermediate products (IX): its stability undergoes a marked decrease after removal of the electronegative carbonyl group. The intermediate furanol (IX), in which the stability of the ring should be significantly lower than in furan itself, can readily undergo transformation involving the diene system and with cleavage of the ring. This is consistent with its ready oxidation via the peroxide (VIII) to formylacrylic acid (XIIIa) and the tautomerisation into the lactones (XI) and (XII) of but-2- and -3-enoic acids. The oxidative and hydrolytic changes undergone by the lactones and the furanol yield 4-oxobut-2-enoic (XIII—XIIIa) and γ-oxobutyric (XV) acids, which are converted by excess of hydrogen peroxide into succinic, maleic, and fumaric acids. The mechanism of the changes undergone by furanol and its tautomeric forms will not be considered here.

1. Role of Complex Formation

Various factors can influence the redistribution of electron density in oxo-derivatives of furan; these produce significant changes in their reactivity. Thus the self-association of 2-furaldehyde and association in its binary systems with the solvent and with hydrogen peroxide cause significant polarisation of the carbonyl group and affect its reactions with this reagent and with peroxyacids. The tendency of furaldehyde to associate[108] is such that its molecules are associated even in benzene[109], although the interaction is then weaker than for ordinary hydrogen bonds. It is not associated in dilute (<0.02 M) solutions. The tendency of furaldehyde to associate is indicated by its abnormally high boiling point in comparison with furan and its great solubility in water, as well as by significant differences in the ultraviolet and infrared spectra in various solvents[60,107,110]. Its self-association and its association with the solvent have been confirmed cryoscopically[112-115]. Weak hydrogen bonds are formed with acetic acid, and stronger bonds with stronger acids[115,116]. Complex formation between furaldehyde and pyromucic acid has been detected polarographically[5]. With sulphuric acid furaldehyde and its derivatives form complexes, which are completely converted into the initial aldehydes when the solutions are diluted[5]. No common view is held on the structure of the complexes. There is no doubt, however, that interaction in furaldehyde–solvent systems does not involve the ring but the carbonyl group. This is indicated by the constancy of the $\nu C:C$ band of the furan ring (1565 cm^{-1}) and the variation in the $\nu C:O$ band in the infrared spectra of furaldehyde obtained in various solvents[107]. Comparison of the infrared spectra of furaldehyde and its solutions in non-polar and in polar solvents shows (Table 1) a change in the structure of the doublet at 1660–1690 cm^{-1} representing vibrations of the carbonyl group involved in hydrogen bonding.

Considerable shifts in the $\nu C:O$ bands are also observed when water and hydrogen peroxide are dissolved in furaldehyde, indicating considerable association in the binary systems. These observations have also been confirmed by cryoscopic measurements: when increasing quantities of hydrogen peroxide are added to a solution of furaldehyde in benzene, the freezing-point depression diminishes, indicating the bonding of furaldehyde molecules by hydrogen peroxide molecules and their removal from solution as complexes[8,117]. Association is more marked with hydrogen peroxide than with water; this is confirmed by the greater solubility, exceeding that in water by a factor of ~3.5.[4]

The strong association in the furaldehyde–hydrogen peroxide system shown by the above facts is consistent with the assumed formation of the intermediate complex (II) (Scheme 7) governed energetically by the stability of the resulting ring. Although the structure of the complex is open to discussion, the fact of its formation is indisputable. Polarisation of the carbonyl group by the hydrogen peroxide molecule must be taken into account in connection with the mechanism of the oxidation of furan oxo-compounds, and by the acid molecule or the proton in acid catalysis [cation (I) in Scheme 7]. Subsequent stages of the reaction will be facilitated significantly by such activation of the molecule.

Table 1. Dependence of stretching frequencies $\nu_{C:O}$ of 2-furaldehyde[107] on nature of solvent.

No.	Solvent	c, M	$\nu_{C:O}$, cm^{-1} [a]
1	None	—	1670 1630
2	Tetrachloro-methane	0.60 2.00	1690 1675
3	1,4-Dioxan	0.60	1685 1670 1635
		1.00	1685 1670
4	Diethyl ether	0.60	1685 1670 1635
		1.00	1685 1670
5	Water[b]	0.50	1680 1670
		6.00	1635
6	Hydrogen peroxide[b]	0.40	1680 1665
		0.80	1630
		4.00	1670 1635
		6.80	1680 1665
		7.90	1630

[a] The most intense band is underlined.
[b] Water and hydrogen peroxide in furaldehyde.

2. Role of Peroxy-compounds

The formation of peroxy-compounds was not even mentioned in the early papers on the oxidation of carbonyl derivatives of furan by hydrogen peroxide and peroxy-acids (Schemes 1–3). Various organic peroxides have since been detected among the products of the oxidation of furan aldehydes and ketones by hydrogen peroxide in the experimental verification of Scheme 7.[118,125] Originally only the total organic peroxides could be determined quantitatively, and the composition qualitatively[118,120-123].

For a long time it proved impossible to isolate the intermediate peroxy-compounds as individual species because of their tendency to detonate. They were stable in solution, but detonated on concentration (cf. the properties of the "active" and "inactive" forms of acyl hydroperoxides[126-130]). By the use of highly concentrated hydrogen peroxide under special conditions it has proved possible to prepare α-hydroperoxyfurfuryl alcohol (III)[18,126,131] and its ring-substituted nitro-derivative[16], which was stable unlike (III) but resembling other peroxides having electronegative substituents[119]. The synthetic compound (III) was identical with one of the peroxides detected among the oxidation products[120,126]. In the active period of oxidation in water the only intermediate peroxy-product is (III). The oxidation of furaldehyde in water involves intermediate formation of this peroxide. Formic, oxo, and furancarboxylic acids accumulate only after it has been transformed. During oxidation in anhydrous media (III) is accompanied by (IV), which predominates when the reaction is conducted in an alcohol[126].

The peroxide (III) is extremely unstable both in aqueous solution and in the crystalline state, decomposing with the formation of furaldehyde, hydrogen peroxide, the peroxide (IV), formylacrylic, maleic, formic, and pyromucic acids, and non-acidic products. The corresponding peroxide from nitrofuraldehyde is quite stable at +5°C, but when heated in water undergoes quantitative conversion into nitrofuran-2-carboxylic acid[18]. In aqueous solution this acid is accompanied by nitrofuranal and hydrogen peroxide. The formation of furaldehyde, its nitro-derivative, and hydrogen peroxide among the products from these hydroxy-hydroperoxides results from their dissociation into a furaldehyde and hydrogen peroxide. This process takes place both during the reaction and when samples of the oxidation products are diluted with water[8]. All the remaining products formed from (III) result from its conversion into (IV), (VI), and (VII). Conversion into furyl formate (VII) is assumed to involve a sextet rearrangement of the Baeyer–Villiger–Criegee–Waters type. Furancarboxylic acid can be formed not only from (III) but also by breakdown of the dihydroxy-peroxide (IV).[126,131] The direction of the rearrangement for furan hydroxy-hydroperoxides is determined by the structure. Electron-accepting substituents cause marked weakening of the π-donor properties of the furan ring, and its migration to the peroxide oxygen atom depleted in electrons becomes impossible. Hydrogen is then more mobile, and the hydroxy-hydroperoxide rearranges to the corresponding furancarboxylic acid (VI), perhaps via (V). Peroxides of furaldehyde itself, its homologues, and derivatives having electron-donating substituents rearrange preferentially into furyl formate (VII).

It is noteworthy that furancarboxylic esters are not detected among the oxidation products of acetylfuran and its derivatives[125]. Independently of the substituents in the furan ring, it obviously migrates in preference to the methyl group during the rearrangement, and furyl acetates are formed. A similar phenomenon has been observed among ketones of the benzene series[30,65,132]. Very small quantities of three further peroxides besides (III) and (IV) have been detected qualitatively in the aqueous oxidation products at the later stages of oxidation[8]. They have been regarded as formed from intermediate products—(IX), (XI)–(XIII), and (XV)—and could not be isolated or prepared in individual form.

Furoyl peroxide and hydroperoxide are not formed in the oxidation of oxo-derivatives of furan by hydrogen peroxide and peroxy-acids. Their presence could easily have been detected from their intense absorption maxima at 262 and 240 nm respectively[119,133], as well as by chromatography[119]. When furaldehyde is oxidised by hydrogen peroxide in water the products do not absorb in the range 240 to 265 nm; in anhydrous media a band is observed at 243 nm, which is due to pyromucic acid[17,126], formed only after breakdown of the organic peroxides.

In order to assess the mechanism of the action of hydrogen peroxide on oxo-derivatives of furan it is important to determine the kinetics of the stage in which peroxides are formed. Oxidation in water cannot be arrested at this stage [120,122,123]. Because water is present, the process goes so far as the formation of acids (Scheme 7), whose accumulation catalyses both the formation and the transformation of the peroxy-compounds, and the final content of organic peroxides is only 0.5–1 g-equiv. litre^{-1}. The kinetic curves representing their accumulation and conversion pass through three maxima. A similar pattern is observed in the oxidation by aqueous hydrogen peroxide of several furan aldehydes [120,124] (methylfuranal, 2-furaldehyde, and its amino- and halogeno-derivatives) and ketones [125] (acetylfuran and its derivatives).

In the absence of acids oxidation in anhydrous solvents ceases at the stage of formation of peroxy-compounds [111,120,126]. The rate constant for the consumption of furaldehyde corresponds to that for accumulation of the organic peroxide [120]. Oxidation in alcohol is a third-order reaction—of the first order with respect to furaldehyde and of the second order with respect to hydrogen peroxide [126]—which is consistent with formation of the hydroxy-hydroperoxide via the complex (II) involving three molecules. If formation of the peroxide is controlled by conversion of the transition complex, the overall process should be described by a third-order equation, as is the case. In the presence of acids the reaction is first order with respect to hydrogen peroxide, which confirms the catalytic role of hydrogen peroxide in the absence of acids.

The above results on the composition and reactions of the intermediate hydroxy-hydroperoxides in the action of hydrogen peroxide on furan oxo-compounds support Scheme 7. However, they still cannot indicate whether conversion of the oxo-compounds into peroxides takes place by a homolytic, heterolytic, or molecular mechanism.

Neither the changes undergone by furaldehyde and hydrogen peroxide nor the accumulation and transformation of organic peroxides and acids in this reaction are influenced by molecular oxygen [134]: the processes are identical in its presence and after it has been completely removed. Breakdown of the organic peroxides is not accompanied by the evolution of oxygen. These facts indicate that, as in most radical oxidations, molecular oxygen plays no part in the oxidation of furaldehyde and its derivatives by hydrogen peroxide. The formation of peroxy-acids and diacyl peroxides characteristic of radical processes is not observed [135,136]. In the autoxidation of furaldehyde, in which radical reactions predominate in the early stages, the initial products of the action of molecular oxygen are furoyl hydroperoxide and difuroyl peroxide [135,137], which are not formed in the oxidation of furaldehyde by hydrogen peroxide [4,126], as mentioned above.

The reacion is accelerated neither by ultraviolet nor by ultrasonic irradiation [4,123,140]. If the formation and transformation of the organic peroxides occurred homolytically, exposure would produce a marked change in its rate [136,138], but some specific effect on the direction of the process merely occurs. This ultraviolet irradiation increases the yield of 4-oxobut-2-enoic acid, and fumaric acid appears [4,123]. Treatment with ultrasonic vibrations results in considerable quantities of malic acid among the oxidation products [14,139,140], as a consequence of ultrasonic initiation of the breakdown of hydrogen peroxide and water with the formation of hydroxyl species [138]. If formation of the peroxide (III) had involved hydroxyl radicals or hydroxide ions, ultrasonic exposure should have intensified the process significantly, but this is not observed.

It is evident that neither molecular oxygen nor hydroxyl species are involved in the formation of (III). The oxidant giving the hydroxy-hydroperoxide must thus be the hydrogen peroxide molecule or ion H_2O_2 or OOH^- (Scheme 7). As the process exhibits no clear sign of a homolytic chain reaction, it cannot be regarded as a radical reaction. Furthermore, a heterolytic or molecular mechanism is suggested by many factors—those mentioned above together with the action of acids and water, the influence of the nature of the solvent, and the electronic effects of substituents in the furan ring.

In the oxidation of furan aldehydes and ketones by hydrogen peroxide the conversion of starting materials and intermediates becomes more intense as acids accumulate in the reaction mixture [4,6,122,123]. Neutralisation of the acids among the oxidation products slows the process down. The oxidation of oxo-derivatives of furan by hydrogen peroxide is evidently catalysed by the acids formed.

The addition of mineral and organic acids to the reaction mixture increases the rate of formation of peroxy-compounds, as can be assessed from the consumption of furaldehyde or acetylfuran. Acids also have a significant influence on the rate of subsequent stages (Scheme 7), as well as on the direction of the process [1,4,141]. Additions of formic, acetic, maleic, succinic, and sulphuric acids [4,6] all increase the consumption of furaldehyde or acetylfuran and hydrogen peroxide, and shorten or completely eliminate the induction period. The catalytic effect of the acid is greater the higher its dissociation constant:

sulphuric > maleic > formic > succinic.

The effect is greatest in the initial stages of the reaction. Such a strong effect of acids on the rate shows that the oxidation of furaldehyde and acetylfuran by hydrogen peroxide is ionic or molecular in character. Further evidence in support of this conclusion is the significant dependence of the rate and the direction of oxidation on the nature of the solvent [2,4,17,107,120,126,141,142].

The oxidation of furan oxo-compounds by hydrogen peroxide in anhydrous media or with a small water content differs significantly from oxidation in water: in the former case the reaction almost stops at the stage of formation of peroxides, and little or no acid is formed. As compared with water, alcohols, and organic acids, protophilic solvents (dioxan, oxolan, pyridine, ethers) slow down markedly the formation of hydroxy-hydroperoxides. Solvents having pronounced protogenic properties (formic and acetic acids) cause strong formation and transformation of (III) (Scheme 7). Initially reaction in alcohols is more intense than in water, after which it slows down. Small quantities of water have a peculiar effect: comparison of the consumption of furaldehyde and the accumulation of peroxides on oxidation in water and in aqueous ether shows that the presence of up to 5% of water in the reaction mixture accelerates the reaction in the initial period; higher water contents retard the process [142] (cf. Table 2).

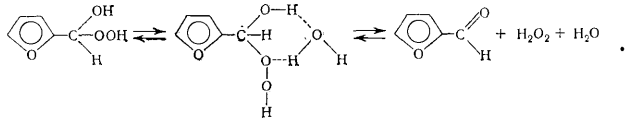
The action of water in the initial stage (Scheme 7) may be to affect either formation of the complex of furaldehyde with $2H_2O_2$ or the dissociation of (III) into furaldehyde and hydrogen peroxide. A high content of water in the oxidation products results in formation of a monohydrate of furaldehyde [107]. Competition in complex formation with furaldehyde between water and hydrogen peroxide molecules delays formation of a peroxide. A similar effect is possible in the presence of excess of water, because the dissociation of (III) into furaldehyde and hydrogen peroxide

is accelerated (Scheme 8). Small quantities of water activate the oxidation of furaldehyde by hydrogen peroxide, mainly by accelerating further transformations of the hydroperoxide (III).

Table 2. Effect of quantity of water on consumption of furaldehyde (Fu) on oxidation with 50% hydrogen peroxide (Fu : H_2O_2 = 1 : 2.2 at 22°C).

Solvent	10^4k_1, min^{-1}
Water	≈0.00
Ether + 0.80% H_2O	21.4
Ether + 1.40% H_2O	34.6
Ether + 3.60% H_2O	59.8

Scheme 8



The nature of the solvent governs not only the rate but also the direction of the process. It has been shown above that the $\alpha\alpha'$-dihydroxy-peroxide (IV) is formed together with (III) in anhydrous and aqueous organic media. The nature of the conversion products of the peroxides varies in anhydrous media: thus the yield of the furancarboxylic acid (VI) is ~50% in alcohols, but only 2% in water[4,120,126]. This reaction is influenced by the polarity and the protophilic or protogenic character of the medium. Such a considerable solvent effect may be expected for ionic or molecular reactions[143]. The influence of solvents on radical reactions would be opposite to that found, since solvents capable of forming hydrogen bonds or π-complexes with radicals terminate the kinetic chain and lower the rate of oxidation[129,144,145]. In the present case alcohols and organic acids, which readily form hydrogen bonds, accelerate the oxidation of furan oxo-compounds by hydrogen peroxide.

A molecular or ionic mechanism is indicated not only by the above experimental results but also by the electronic effect of substituents in the furan ring on the rate and direction of the reaction. The effect on the rate has been assessed[120,124-126] by oxidising a series of aldehydes and ketones with a substituent—methyl, chloro, bromo, iodo, dialkylamino, hydroxymethyl, nitro—at position 5 in the furan ring. This series has the same reactive centre—the carbonyl group—and a variable 5-substituent. Conducting the reactions in a solvent containing a small quantity of water and at a relatively low temperature (30 to 40°C) enabled the process to be arrested at the stage of peroxide formation. The quantitative results given below relate to this particular stage. Its direction and mechanism were unaffected by the choice of solvent: in all cases the hydroxy-hydroperoxide (III) was formed with the substituent at position 5 in the heterocycle. Electron-donating substituents (methyl, dialkylamino) tend to increase the oxidation rate constant, whereas electron-accepting substituents (nitro, hydroxymethyl) tend to diminish the rate (Table 3). In contrast to methyl, hydroxymethyl retards oxidation[4]. Hydroxymethylfuraldehyde is oxidised rather more slowly than furaldehyde itself ($\tau_{1/2}$ = 63 and 55 min).

Table 3. Rate constants for the oxidation of 5-substituted furaldehydes[120] (aldehyde : H_2O_2 = 1 : 10 at 40°C) and acetylfurans[6] (ketone : H_2O_2 = 1 : 50 at 30°C) in aqueous dioxan.

5-Substituent	Aldehydes			Ketones		
	10^3k, min^{-1}	$\lg\frac{k}{k_0}$	σ	10^3k, min^{-1}	$\lg\frac{k}{k_0}$	σ
I	9.90	−0.1209	0.276	6.20	0.3898	−0.130
Br	11.50	−0.0555	0.232	8.30	0.5160	−0.220
H	13.00	0.0000	0.00	2.52	0.000	0.000
Cl	15.00	0.0607	−0.227	63.60	1.4004	−0.240
Me	25.00	0.3010	−0.170	10.20	0.6055	−0.120
NMe_2	29.90	0.3617	−0.205	—	—	—

The oxidation of halogenated furan oxo-compounds follows a curious course in aqueous dioxan. That of ketones by hydrogen peroxide is accelerated by all the halogens examined at position 5 of the furan ring, with chlorine more effective than bromine, and iodine the least effective. Oxidation of the aldehydes is accelerated by chlorine, but somewhat retarded by bromine and iodine. All the halogens accelerate the oxidation of furaldehyde in anhydrous media[126]. The reason is that, during the reaction, the positive conjugation effect of the halogens becomes stronger in comparison with their negative inductive effect. This is already observed in the parent substance as a result of the strong acceptor properties of the carbonyl group. The ultraviolet and infrared spectra of substituted furan oxo-compounds provide convincing support[6]. Under the influence of the polarised carbonyl group the positive conjugation effect of the halogen increases many times during the reaction. Similar phenomena are observed in the electrophilic substitution of halogenated benzenes[143]. The greatest positive conjugation effect is found[146] with chlorine, and diminishes in the sequence Cl > Br > I; it is explained by the most favourable overlap of electrons in the 3p shell of chlorine with 2p electrons of carbon.

It is remarkable that this effect of halogens has not been observed among acetophenones: the rates of oxidation of p-chloro- and p-bromo-acetophenones by peroxy-acids are lower than those of acetophenone[147]. This shows that the transmissibility of electronic effects through the benzene ring differs from their transmissibility through the heterocyclic furan system: the π-electrons of furan are more mobile. A complete analogy cannot, of course, exist in the oxidation of benzene and furan carbonyl compounds by hydrogen peroxide and peroxy-acids.

The positive conjugation effect of halogens is more strongly developed in substituted acetylfurans than in furaldehyde and its derivatives, owing to the greater interaction of p-electrons of the halogens with those of the furan ring in ketones. The π-electron density of the furan ring is less displaced by the ketone group, being a weaker acceptor than the aldehyde group, and better conditions are created for interaction of electrons of chlorine and the ring. On the other hand, more intense polarisation of the carbonyl group is required during reaction with ketones

than with aldehydes, which tends to strengthen the positive effect of halogens. The difference in degree of conjugation of halogens in furan aldehydes and ketones develops mainly in the reactive state, since the infrared spectra indicate no special difference in the static state [6]. The effects of substituents are more strongly developed in the oxidation of furan aldehydes by hydrogen peroxide in aprotic solvents of low polarity (dioxan, oxolan), and are extremely slight in alcohol [126].

Migration of electrons towards the reactive centre—the carbonyl group—evidently governs the rate of oxidation of furan oxo-compounds by hydrogen peroxide. Hence the formation of (III) is a result of electrophilic attack, which apparently consists in protonation of the carbonyl group. Conjugation of π-electrons of the ring and the group diminishes the δ^+ charge on the carbonyl carbon, so that nucleophilic attack by such a weak nucleophile as hydrogen peroxide requires preliminary polarisation of the carbonyl by a proton. Hydrogen peroxide and the solvents used (water and alcohols) are extremely weak acids, which is responsible for the slowness of the electrophilic stage [143]. If the acidity of the solvent is closely similar to that of hydrogen peroxide, the solvent may act as protogenic substance, as in the oxidation of furaldehyde by hydrogen peroxide in water [142]. In less acidic media hydrogen peroxide acts as the acid [126].

The rate of oxidation is affected not only by substitution at the 5-position in the furan ring but also by change in the character of the side-chain containing the carbonyl group. Furylacrylaldehyde is oxidised very easily, but oxidation begins at the unsaturated side-chain, and the primary reaction products are furaldehyde and oxalic acid. The furaldehyde then undergoes conversion by the usual scheme [4]. This example clearly demonstrates that the oxidation of furan oxo-compounds containing electron-accepting substituents does not start at the furan ring, and that the ring is more stable than the double bond in the side-chain. Acetylfuran is oxidised considerably more slowly than is furaldehyde [125]: thus with 50% hydrogen peroxide at 60°C and the reactants in the proportions 1 : 2.5 furaldehyde is oxidised more rapidly than acetylfuran by a factor of 20 (the respective half-conversion times are 23 and 450 min). Substitution of the aldehydic hydrogen by methyl produces no great change in the distribution of electron density in the furan ring, as is indicated by the close similarity of the ultraviolet and infrared spectra of acetylfuran and furaldehyde [6,148]. The infrared spectra reveal no difference in position or intensity of the absorption bands due to stretching and deformation vibrations of the furan rings in aldehyde and ketone; appreciable differences are shown only by bands due to the carbonyl group.

The introduction of alkyl substituents increases the electron density on the carbonyl group and should thereby improve its sensitivity to electrophilic attack. This is accompanied by a diminution in the tendency of the carbonyl carbon to interact with nucleophilic reagents, owing both to electronic and to steric factors. The stage of hydroxy-hydroperoxide formation is limited by electrophilic attack with both aldehydes and ketones (Table 3). The unexpected sharp decrease in rate of oxidation with acetylfuran compared with furaldehyde can be explained if the formation of (III) is regarded as a termolecular reaction. The plausibility of this hypothesis has been demonstrated for furaldehyde [126]. The nucleophilic stage may be slower with ketones, resulting in a fall in the overall rate of oxidation. The electronic effects of substituents in the furan ring, like other factors, suggest an ionic or a molecular mechanism of the formation and transformation of hydroxy-hydroperoxides in the oxidation of furan oxo-compounds by hydrogen peroxide.

3. Furyl Formate and its Conversion Products

Furyl formate and the homologous acetate are intermediates in the oxidation of furaldehyde and acetylfuran by hydrogen peroxide (Scheme 7). They have been isolated individually, which convincingly proves the suggested rearrangement of the hydroxy-hydroperoxide (III) into (VII).

Formation of these compounds when furan oxo-compounds were treated with hydrogen peroxide and peroxy-acids had previously been ignored (Schemes 1–3), and no attempts had been made to isolate them from the oxidation products. Furyl formate (VII) was first isolated from the products of the oxidation of furaldehyde by hydrogen peroxide when they were evaporated down or at the start of vigorous reaction [15]. Furyl formate is comparatively easily hydrolysed to formic acid (X), the butenolides (XI) and (XII), and 4-oxobutyric acid (XV), and oxidised to 4-oxobut-2-enoic acid (XIII). [8,15] Accumulation and transformation of these products are observed in the oxidation of furaldehyde by hydrogen peroxide, which has been investigated quantitively [4,8,126]. The rate of accumulation of formic acid when furaldehyde is oxidised in water [120] clearly shows that intense formation of the acid ensues after considerable quantities of furaldehyde have been consumed. This is fully consistent with the characteristics of the consecutive reaction represented in Scheme 7.

The furanol (IX) formed by the hydrolysis of (VII) is too unstable to be detected among the oxidation products [54]. For this reason furanol has not yet been prepared in any other way. However, its stable tautomers—the butenolides (XI) and (XII)—have been isolated in large quantities [8,57]. Products of the extensive transformation of furanol—4-oxobutyric and 4-oxobut-2-enoic acids—are formed in this reaction [1,10,12,126]. Accumulation of the aldehydic acids suffers a delay, the maximum occurring only after 2 h, when the furaldehyde is almost completely exhausted. The oxo-acids formed undergo vigorous oxidation to succinic and maleic acids (XVI) and (XIV), which have been isolated from the oxidation products [1,3,14,17]. The same acids are formed when furaldehyde is oxidised by peroxy acids [26,28], which indicates the same mechanism of oxidation as with hydrogen peroxide.

Furyl acetate could not be isolated from the products of the oxidation of acetylfuran by hydrogen peroxide, because it is oxidised much more rapidly than the initial ketone [149]. However, its formation and transformation during the reaction have been demonstrated qualitatively [149–154]. The processes occurring in the oxidation of acetylfuran are analogous to the hydrolytic and oxidative changes undergone by furyl formate (VII) and shown in Scheme 7, except that hydrolysis of furyl acetate yields acetic acid. These results show that rearrangement of the peroxide (III) into (VII) does actually take place.

Formation and transformation of the peroxides have been most fully studied in the complicated consecutive reaction of furan oxo-compounds with hydrogen peroxide. The occurrence of the remaining stages has been proved by the products, but their mechanism has not been investigated in detail. This is due to the peculiarities of the reaction: when oxidation occurs in water, individual stages cannot be isolated, nor can autocatalysis by the resulting acids be taken into account; in anhydrous media

the reaction effectively ceases at the stage of peroxide formation. The rate of conversion of (III) could not be estimated because of the accumulation of other peroxides. In view of the properties of (III), however, the process can be regarded as fairly rapid [18]. It is strongly exothermic [155].

Thus the regularities found in the reaction and the intermediate and final products identified permit Scheme 7 to be accepted as soundly based both theoretically and experimentally for the oxidation of furan oxo-compounds by hydrogen peroxide. It is very useful to estimate the activation parameters of the reaction in order to interpret its mechanism.

V. ACTIVATION CHARACTERISTICS OF THE PROCESS

The thermal effects of individual stages and of the overall oxidation of furaldehyde by hydrogen peroxide have been found by calculating the energies of formation of the products on the basis of approximate additivity [120,156,157]. The conjugation energy of furaldehyde and other furan compounds has been taken into account at the stage of their transformation [48,53]. The method used is arbitrary, since it allows for neither the complete interaction of atoms in the molecules nor the effects of the medium. However, the results are useful for estimating the thermal effects.

Table 4 shows that the oxidation of furaldehyde by hydrogen peroxide is exothermic, which has been confirmed experimentally [3,123]. The greatest quantity of heat is evolved during the conversion of peroxy-compounds [155], which is consistent with the results in Table 4 (stages *2*, *5*, and *8*). Calculation of the thermal effects shows the largest consumption of energy at stages *3*, *4*, and *6*. However, the experimental conditions require the significant corrections to be made to these results. Excess of water in the oxidation products, catalysis by the accumulating acids, and conversion of the reaction products in the later stages (*4*–*8*) promote ready hydrolysis of furyl formate when the process is conducted in water. This explains the low yields when furyl formate is isolated. The limiting stage in processes *1*–*8* is most probably formation of the hydroxy-hydroperoxide (stage *1*).

Table 4. Energies of formation of molecules and heats of oxidation of furaldehyde by hydrogen peroxide.

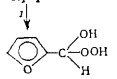
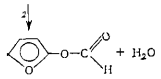
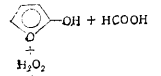
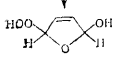
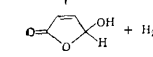
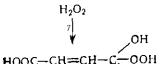
Stage	Energy of formation, kcal mole^{-1}	Heat of reaction, kcal mole^{-1}
	1121.0	
H_2O_2	240.2	
1		−15.1
	1376.3	
2		−50.0
	1188.0+238.2	
+ H_2O	238.2	
3		+54.0
	991.2+381.0	
+ H_2O_2	240.6	
4		+23.5
	1208.3	
5		−88.1
	1058.2+238.2	
6		+23.0
HOOC—CH=CH—CHO	1035.2	
+ H_2O_2	240.6	
7		−16.7
	1292.5	
8		−88.1
HOOC—CH=CH—COOH + H_2O	1142.4+238.2	
	total	−157.5

Table 5. Activation parameters [120,126,158] of the oxidation by hydrogen peroxide of furaldehyde (Fu) (30% H_2O_2 with Fu : H_2O_2 = 1 : 15) and acetylfuran (AF) (50% H_2O_2 with AF : H_2O_2 = 1 : 3).

Activation parameter	Furaldehyde in		Acetylfuran
	water	alcohol	
Apparent activation energy E, kcal mole^{-1}	11.4	20.5	21.9
Pre-exponential factor A at 60°C, s^{-1}	$8.5 \cdot 10^{-5}$	$7.4 \cdot 10^{11}$	$5.1 \cdot 10^{11}$
Free energy of activation $\Delta G^{\neq}$ at 60°C, kcal mole^{-1}	24.7	24.7	25.7
Enthalpy of activation $\Delta H^{\neq}$ at 60°C, kcal mole^{-1}	10.7	19.8	21.2
Entropy of activation $\Delta S^{\neq}$ at 60°C, cal deg^{-1} mole^{-1}	−41.3	−14.6	−13.7

The experimental activation parameters of such complicated reactions as the oxidation of furan oxo-compounds by hydrogen peroxide (Table 5) apply in effect to the limiting stage of the process. As shown above, in water this is the stage of conversion of the carbonyl compound into a hydroxy-hydroperoxide. Oxidation in an anhydrous medium ceases at the first stage. The comparatively low activation energies are consistent with thermochemical calculations (Table 4) and the observed exothermic character of the process. The high activation energy for acetylfuran in comparison with furaldehyde corresponds to the above features of its oxidation. The lower activation energy of oxidation in water than in alcohol is consistent with the above role of water in the reaction. The experimental enthalpies of activation are closely similar to those calculated for the first stage in Scheme 7 (Table 4).

The low values of the pre-exponential factor (according to collision theory $A \simeq 10^{13}$ s^{-1}) suggest that the molecules are in contact and that the transition state is polar. The considerable degree of order of the transition state with loss of its rotational and translational degrees of freedom, as well as its polarity, is confirmed by the negative entropy of activation, which is possible in a system having a cyclic activated complex [159].

The autocatalytic character of the process is confirmed by the low entropy of activation [160]. The conclusion that, when oxidation takes place in water, the active stage is catalysed by acids accumulating during the reaction is supported by the identity of the activation energies for the oxidation of acetylfuran with and without acid catalysis [6], as well as by the lower activation energy in water than in alcohol (Table 5). Like the other experimental results cited, the activation parameters indicate that the action of hydrogen peroxide on furan oxo-compounds involves a transition complex and is autocatalytic.

Thus the investigations surveyed above indicate that the mechanism of the reaction of furan oxo-compounds with hydrogen peroxide and peroxy-acids represented by Scheme 7 is soundly based both experimentally and theoretically. The regularities elucidated in its occurrence and the effects of various factors permit this complicated consecutive and parallel process to be controlled with the aim of obtaining the most important products [1-18].

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Dextran and Its Derivatives

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The Review covers the physicochemical properties of dextran, the preparation of various types of derivatives, and the study of their properties and possible fields of application. Consideration is given also to the preparation of dextranates of alkali and alkaline-earth metals, complexes of dextran with multivalent metals, oxidation products of dextran and their derivatives, deoxy-derivatives, esters and ethers, dextran derivatives having a three-dimensional cross-linked structure, graft copolymers, and derivatives containing chemically attached medicinals. The production of many of the above derivatives is shown to extend considerably the possible applications of dextran. A list of 335 references is included.

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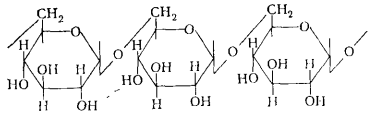
I. INTRODUCTION

"Dextran" is the group name for polysaccharides, obtainable by microbiological synthesis, whose main molecular chain consists of anhydro-D-glucopyranose units linked predominantly by α-1,6-glycosidic bonds



The macromolecules of various dextran preparations may contain also various quantities of α-1,2-, α-1,3-, and α-1,4-glycosidic bonds, by means of which side-chains are usually attached to the main chain. Dextrans have been obtained whose molecules are almost entirely unbranched, while the monomer units are 95% linked by α-1,6-glycosidic bonds.

Dextran is obtained from cultures of the micro-organisms—*Leuconostoc mesenteroides*, *Leuconostoc dextranicum*, *Streptobacterium dextranicum*, etc.—in a medium containing sucrose or other carbohydrates in which anhydro-D-glucopyranose units are present, including a dextran of low molecular weight. The product of microbiological synthesis is termed "native dextran".

Many strains of the above micro-organisms exist, and produce dextrans differing in structure and properties, i.e. in molecular weight, degree of branching of the macromolecules, relative contents of particular types of glycosidic links, solubility, optical activity, and physiological action. The molecular weight of native dextran is usually lowered by acid hydrolysis, generally with simultaneous decrease in the degree of branching of the macromolecules.

The polysaccharide dextran has become widely known because aqueous solutions of certain preparations of molecular weight $(35-70) \times 10^3$ and low degree of branching are effective substitutes for blood plasma. The advantage of dextran over carbon-chain polymers also employed for this purpose (polyvinylpyrrolidone, polyvinyl alcohol) consists in its gradual hydrolysis by enzymes in the organism. This eliminates the danger that the polymer will accumulate in organs of the macro-organism. A very important use of dextran is as starting material for the production of Sephadexes, which are widely employed in gel chromatography. Dextran and its derivatives are finding increasing applications for other purposes.

The microbiological synthesis, structure, biological properties, and application of the polysaccharide in medicine have been described in detail in reviews and monographs[1-13]. However, no systematic surveys have been made of the physicochemical properties of dextran and the preparation and properties of its derivatives. The present Review covers work published mainly during the past decade.

II. PHYSICOCHEMICAL PROPERTIES OF DEXTRAN AND ITS APPLICATION

Native dextran is a polymer of high molecular weight (reaching 10^7-10^8) and high polydispersity ($M_w/M_n = 10^2-10^3$).[14] Information on the determination of the molecular weight of native dextran will be found in Refs. 15 and 16.

The molecular weight of native dextran can be reduced by acid hydrolysis[17,18], enzymic depolymerisation[19], alcoholysis[20], thermal degradation[21], treatment with hydrogen peroxide[22], γ-irradiation[23-26], ultraviolet and X-ray irradiation[27,28], and the action of ultrasonic vibrations[29]. Under industrial conditions acid hydrolysis is used for this purpose. The nature of the acid—hydrochloric, perchloric, nitric, sulphuric, or orthophosphoric—has little effect on the quantitative proportions of the hydrolysis products[17]. Hydrolysis followed by fractionation enables the ratio M_w/M_n to be reduced to 1.2-1.5. Acid hydrolysis results also in a diminished degree of branching of the

dextran macromolecules, owing to the relatively high stability of the α-1,6-glycosidic bond to acid hydrolysis. A systematic investigation has been made by electron spin resonance of the nature of the radicals formed when dextran is exposed to ultraviolet radiation, X-rays, and γ-rays, and of the kinetics of their accumulation and destruction[24,25,27].

Partly hydrolysed dextran can be fractionated and its polydispersity determined by fractional precipitation from solution on addition of an oxidising agent[30,31], gel permeation using Sephadexes[32-35] and other gels[36-39], filtration through microporous membranes[40], and turbidimetric titration[41]. It dissolves in water, formamide, and dimethyl sulphoxide; various alcohols and acetone do not dissolve dextran, but precipitate it from solution.

Many physicochemical researches have been aimed at establishing a relation between the properties and the structure of dextran preparations. The infrared absorption band at 794 cm^{-1}, due to the presence of α-1,3-glycosidic links in the macromolecules, varies in intensity in the spectra of dextrans formed by different micro-organisms[42]. Measurement of the intensity has been used to determine the content of this type of glycosidic link in various dextran preparations[43]. The conformation of the monomer unit of carbohydrates has a significant influence on the infrared spectrum in the range 700–1000 cm^{-1}. Investigation of this region in the spectrum of dextran and its derivatives[44] led to the suggestion that the most probable conformation of the anhydro-D-glucopyranose units in dextran macromolecules is $C1$. Nuclear magnetic resonance and Raman spectra have been determined for dextran[45-47].

Thermogravimetric investigation of the structure of dextran[48,49] reveals endothermic peaks in the range 130–310°C on the thermograms of all the dextran preparations investigated. The peak in the region of 200°C is typical of dextrans containing mainly α-1,6-glycosidic links; the thermograms of dextrans containing a considerable quantity of α-1,3-glycosidic links included a peak near 245°C.

The structure of dextran macromolecules also influences the sorption of water vapour by the polymer[50,51]. The quantity of water sorbed by specimens in which the α-1,6-glycosidic links were accompanied by a considerable number of α-1,3- and α-1,4-bonds increased monotonically with increase in the relative water vapour pressure. With preparations having a high content of α-1,6-glycosidic links the quantity of sorbed water increased with the vapour pressure to 75–85%, after which it decreased. This phenomenon was attributed to crystallisation of the dextran. Preparations whose macromolecules are only slightly branched, with the branches consisting mainly of one or two anhydro-D-glucopyranose units, are evidently able to crystallise. Study of such a preparation[52] by means of an original method for determining the lengths of side-chains established that approximately 40% of the branches contained one glucose residue, 45% contained two residues, and only 15% had a longer chain. Examination of eight different preparations by X-ray diffraction established[53] that all the dextran polymers were amorphous.

During recent years investigations have been made[54,55] on several physicochemical properties of dextran produced in the USSR, obtained by the partial acid hydrolysis of native dextran formed by the strain *Leuconostoc mesenteroides* SF-4 (molecular weight 55 000). X-Ray diffraction and thermomechanical examination have shown that spray-dried dextran is amorphous (glass point 140°C, flow point 180°C), but is able to crystallise when certain temperature–time heat-treatment schedules are used (with relatively slow cooling from 190 to 20°C or with slow heating), and also on treatment with liquids in which it swells (water, formamide)[55]. The possibility of converting dextran into states of rubberlike elasticity and viscous flow is the first observation of these phenomena in polysaccharides. The crystallisation of dextran on heat-treatment and when treated with water or formamide results in the appearance of new absorption bands in the infrared spectrum and in selective increase in the relative intensity of individual bands, which can be explained by the predominance of certain types of rotational isomers that favour crystallisation. The heat of interaction of amorphous dextran with water is 29.5 cal g^{-1}, and the "water surface" calculated from the water-vapour sorption isotherm is 228 m^2 g^{-1}.[54]

Many studies have been made of dextran solutions, an important physical characteristic of which is their optical activity, which depends on the structure of the macromolecules—the content of α-1,3-glycosidic bonds—and on the nature of the solvent[58]. The value of $[\alpha]_D$ for aqueous solutions of various dextran preparations varies from +199° to +235°. Extrapolation to zero content of such bonds gives 194.6°.[56,57] The optical activity of dextran solutions is unaffected by the presence of α-1,4-glycosidic bonds[56,57]. The influence of the solvent on $[\alpha]_D$ has been investigated[58]. Study of the optical rotation of dextran in cuprammonium solution indicates that the monomer units in the dextran macromolecules have the $C1$ conformation[59]. Similar conclusions were reached[60] from an n.m.r. study of a solution of dextran in dimethyl sulphoxide.

Several investigations have been made recently of the interaction of dextran macromolecules with the solvent. The macromolecules of several preparations of native dextrans form structural association complexes with the solvent[61]. The possibility of such association was examined in terms of the helical structure of native dextran stabilised by intramolecular hydrogen bonds and of the character of the hydrogen bonds formed in solution. The form of the macromolecules and the viscosity of aqueous solutions are affected by the presence of other substances: the asymmetry of the macromolecules of native dextran is greater in aqueous solutions of urea and glucose and in concentrated salt solutions than in water, but is less in aqueous methanol[15].

Study of the rheological properties of aqueous solutions of dextran (M_W = 120 000) over a wide concentration range revealed a sharp change at concentrations of 40–43%.[62] This was attributed to the structure of the hydration sheath of the macromolecules: an abrupt change in viscosity occurs when the composition corresponds to the formation of $1\frac{1}{2}$ layers of water molecules around each dextran macromolecule. Nuclear magnetic resonance has been used to study the interaction of water with dissolved dextran macromolecules[63], and electron microscopy to determine the size and configuration of the macromolecular aggregates in solution[64].

Viscosimetry has certain limitations as a method for determining the molecular weight of dextran. The constants K and α in the formula $[\eta] = KM^{\alpha}$ are different for dextran preparations differing in degree of branching or in the proportions of the various types of glycosidic bonds in the macromolecules. Examination of various dextran preparations by light scattering established[65] that, when 15–20 α-1,6-glycosidic bonds are present per glycosidic bond of a different type, the molecular weight of the dextran can be calculated by means of the formula $[\eta] = 0.00218M^{0.43}$; with greater branching of the macromolecules, when the ratio becomes 2–3, the coefficients K and

α are respectively 0.0044 and 0.34. Soviet dextran (polyglucin) preparations conform to the expression $[\eta] = 0.000966M^{0.5}$ over the range of molecular weights 40 000–100 000.[66]

The intrinsic viscosity of aqueous solutions of hydrolysed dextran is increased by the addition of potassium thiocyanate and calcium chloride, but diminished by lithium and potassium chlorides[67]. It depends also on the solution pH.[68] The variation in viscosity is attributed to variation in the character and number of intramolecular hydrogen bonds. The relation between the degree of branching of the macromolecules of dextrans and other natural polymers and the viscosity of their solutions has been studied[69,70]. The effects of the nature of the solvent (water, formamide, aqueous methanol, and aqueous dimethylformamide), the molecular weight of the dextran (M_n = 4100–32 000), and the temperature on the intrinsic viscosity of the solutions have been investigated[71]. Various aspects of the use of viscosimetry to determine the molecular weight of dextran have also been discussed[72–76].

Several papers have also appeared during recent years on the conformational transitions of dextran macromolecules in solution[77], the determination of virial coefficients[72,78], increments of the refractive indices of aqueous solutions of dextran[79], the heat and entropy of mixing of dextran with water over a wide concentration range[78], and the study of osmotic pressure and the scattering of light in aqueous solutions[72,78,80–82].

Applications of Dextran

As mentioned above, dextran is widely used to prepare most effective plasma substitutes for application in shock and the loss of blood; these are manufactured in various countries under the names polyglucin, dextran, Macrodex, Expandex, Intradex, and Dextraven[7]. The use of dextran for the production of Sephadexes is discussed in Section VIII. Other uses of dextran have also been reported—for preparing various forms of medicines (tablets, capsules for pharmaceutical preparations, eye-drops)[83–85], in the foodstuffs industry[86], in drilling, and in the production of cosmetic agents[87]—and the production of fibres from dextran has been patented. As mentioned above, dextran is hydrolysed by enzymes in the organism[88–92], so that considerable interest attaches to obtaining from dextran fibres or other articles (e.g. pins for joining bones in fractures) for use in surgery, when they would be gradually absorbed in the organism.

III. DEXTRANATES OF ALKALI AND ALKALINE-EARTH METALS AND COMPLEXES OF DEXTRAN WITH MULTIVALENT METALS

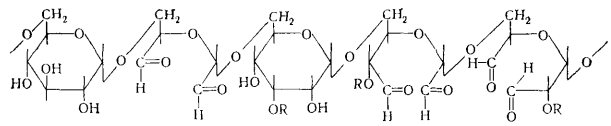
With alkali and alkaline-earth metals dextran forms alkoxides termed "dextranates". Sodium dextranate is produced when dextran is treated with a solution of sodium in liquid ammonia[93,94]; calcium dextranate, containing up to 20% of calcium, can be obtained according to a patent[95] from dextran and a calcium alkoxide of a lower alcohol. Dextranates are used as intermediates in the preparation of other dextran derivatives, e.g. its graft copolymers[94] and ethers[93].

Complex compounds of dextran have been described with Cuoxene $[Cu(NH_2CH_2CH_2NH_2)_2](OH)_2$ and Cadoxene $[Cd(NH_2CH_2CH_2NH_2)_3](OH)_2$.[96] The scientific and patent literature contains reports of the formation of compounds of dextran (probably complex) with hydroxides of several multivalent metals—calcium(II), bismuth(III), lead(II), cerium(III), lanthanum(III), chromium(III), aluminium(III), copper(II), cobalt(II)[97–99], and also iron(III)[100–108]—the exact structure of most of which has not been established. They are generally obtained by reaction between dextran and salts of the metals in an alkaline medium (sometimes in the presence of other compounds of low molecular weight, in particular those possessing complexing properties). In some cases dextran is pretreated with a reductant (e.g. sodium tetrahydroborate) or an oxidant (hydrogen peroxide). The largest number of patents and scientific papers deal with the preparation and study of the compound of dextran with iron(III) hydroxide, which is used for the treatment of anaemia in veterinary practice and is produced in several countries. Information is available also on the biological properties of compounds of dextran with hydroxides of other multivalent metals[97,99].

IV. PREPARATION OF OXIDATION PRODUCTS AND THEIR DERIVATIVES

The main lines of development of this branch of the chemistry of dextran during the past decade have been the use of additional oxidants to obtain carbonyl-containing derivatives and the preparation of several new derivatives from oxidation products of dextran.

Complete oxidation with periodic acid has long been used, together with other methods, to study the structure of dextran macromolecules. Investigation of the influence of the conditions of oxidation on the content of formyl groups in the water-soluble reaction product (which can provisionally be named "dialdehydodextran" by analogy with "dialdehydocellulose") showed[109] a high rate of reaction in a homogeneous medium (oxidation was complete in 25 min in the presence of 1 mole of periodic acid per monomer unit). The structure of the product of the partial oxidation of dextran by periodic acid can be represented by



Since the 1740-cm^{-1} band in the infrared spectrum of this polymer is very weak[110], however, it may be concluded that most of the aldehyde groups are not in the free state but probably involved in the formation of acetal, hemiacetal, and hemialdol[110] bonds or are present in the hydrated form. Study of the stability in an alkaline medium (pH $\geq$ 10) of dextran oxidised with periodic acid shows that hydrolysis of the glycosidic links is then accompanied by the Cannizzaro reaction with the formation from two formyl groups of one carboxy- and one hydroxy-group[111,112].

The oxidation of dextran by lead tetra-acetate in dimethyl sulphoxide, which also yields dialdehydodextran, is more rapid than oxidation by sodium periodate in aqueous solution[113]. Oxidation with a mixture of dimethyl sulphoxide and acetic anhydride gives a polymer containing keto-groups[114,115]. Under these conditions oxidation involves mainly hydroxy-groups at position 3 in the monomer unit of dextran[114]. A side-product of oxidation with dimethyl sulphoxide and acetic anhydride is the methylthiomethyl ether of dextran. The aqueous solubility of preparations from this dextran derivative depends both on the degree of

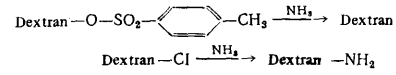
oxidation and on their sulphur content[115]. Water-soluble keto-derivatives can be obtained by oxidising dextran with chlorobenzotriazole[115]. In contrast to dialdehydodextran, the above keto-derivatives are quite resistant to alkaline hydrolysis (pH 9.5 at 20°C).[115]

Dialdehydodextran has been used to prepare derivatives containing carboxy- and amino-groups, the former by oxidation with sodium chlorite[109] and the latter by treatment with liquid ammonia in the presence of Raney nickel under pressure[116]. Degradation accompanying the action of aqueous ammonia on dialdehydodextran at high temperatures leads to the formation of imidazole and 4-methylimidazole[117].

The above dextran derivatives containing formyl, carboxyl, and keto-groups have been used to prepare derivatives containing chemically attached medicinal compounds (isonicotinohydrazide, novocaine, sulphanilamide, serotonin, morphine, Promedol, and various antibiotics)[118-124]. The infrared spectra of several of these compounds have been published[110,115,121]. Intraperitoneal injection of dialdehydodextran enhances the resistance of mice to infection with pathogenic strains of *Escherichia coli* [125, 126].

V. DEOXY-DERIVATIVES OF DEXTRAN

Study of the preparation of deoxy-derivatives of dextran containing halogen, thiol, and amino-groups has begun during recent years. Deoxyiodo-derivatives have been obtained[115] by nucleophilic substitution when dextran is treated with methyltriphenoxyphosphonium iodide and when sodium iodide acts on dextran toluene-*p*-sulphonate or nitrate. The fact that deoxyiododextran having a degree of substitution of 0.71 can be obtained from dextran toluene-*p*-sulphonate shows the possibility of replacing by halogen toluene-*p*-sulphonyloxy-groups attached to secondary carbon atoms in the anhydro-D-glucopyranose monomer unit. A water-soluble chlorodeoxydextran has been prepared by treating dextran with thionyl chloride in dimethylformamide[115,127]. Aminodeoxy-derivatives have been obtained[115,127] by nucleophilic substitution:



A deoxymercapto-derivative of dextran has been obtained by pyrolysis of the product of the oxidation of dextran xanthate with sodium nitrite followed by treatment of the resulting polymer with alkali[128].

VI. DEXTRAN ESTERS

Development of this branch of the chemistry of dextran in recent years has been characterised by the study of new methods for preparing already known esters, the elaboration of methods for obtaining new types of esters (including those containing residues of natural compounds—α-amino-acids and heterocyclic bases present in ribonucleic and deoxyribonucleic acids), and investigation of the properties and possible fields of application of dextran esters.

Esters with Inorganic Acids

The most fully studied ester is dextran sulphate, usually obtained by treating dextran with chlorosulphuric acid in absolute pyridine. Sulphur trioxide, sulphuryl chloride, oleum, concentrated sulphuric acid, and piperidine-*N*-sulphonic acid can also be used[129-134]. The reaction can be conducted in dimethylformamide, formamide, methylpyridine, dioxan, or dimethyl sulphoxide. Treatment of dextran with piperidine-*N*-sulphonic acid dissolved in dimethyl sulphoxide enables a uniformly substituted dextran sulphate to be obtained without significant fall in the degree of polymerisation[133]. The distribution of sulphate groups in the dextran sulphate macromolecule obtained in a heterogeneous system is non-uniform[135].

Alkaline saponification of dextran sulphate followed by complete acid hydrolysis of the product yields not only glucose but also altrose, mannose, and gulose[135,136]. Formation of such monomer units in the polysaccharide macromolecules is due to change in the configuration of the hydroxy-groups accompanying cleavage in an acid medium of the α-oxide rings formed by saponification of the sulphate groups.

Measurement of the viscosity of dextran sulphate solutions of different ionic strengths indicates that the macromolecules are highly flexible[137]. The interaction of dextran sulphate with various inorganic cations and organic cations of low molecular weight has been studied[138-142].

The ability of dextran sulphate to form compounds with various biopolymers enables it to be used to separate, isolate, and purify proteins, nucleic acids, lipoproteins, and viruses[143], and is also the reason for various aspects of its biological activity. Much work has been done on the possibility of using dextran sulphate as a blood anticoagulant. Despite the pronounced effect obtained with a dextran sulphate of high molecular weight, however, the strong toxic action on the organism has prevented its practical application.

During recent years, however, interest has been renewed in the preparation of less toxic forms of dextran sulphate, and in the study of its possible application as a blood anticoagulant[133, 144, 145] and for other purposes in biology, biochemistry, and medicine. The results obtained from investigation of the medicobiological properties of dextran sulphate are summarised below. Dextran sulphate intensifies the antiviral activity of interferon in experiments *in vitro*[146,147], and itself possesses antiviral activity *in vitro*[148-150], but was inactive in experimental influenzal infections of white mice[148,151]. Dextran sulphate inhibits the activity of proteinases[152,153] and lipoprotein lipase[154], when its molecular weight has a significant influence on the degree of inhibition. It is therefore suggested[152] that dextran sulphate can be used to treat gastric ulcers. Products of its reaction with aluminium salts have been patented for this purpose[155,156]. Dextran sulphate possesses antilipaemic activity[130,133], and inhibits the template activity of deoxyribonucleic acids[157] and the respiratory activity of the mitochondria of rat liver cells in a medium of low ionic strength[158]. In the latter case it was assumed that the sulphate prevents the entry of nucleotides into the mitochondria. In experiments on mice spleen cells dextran sulphate inhibited the formation of antibodies on the injection of sheep erythrocytes[159]. It has been proposed also for the preparation of polymeric medicinals[160] and of photographic films[161].

According to the patent literature dextran phosphates can be prepared by the action of phosphoryl chloride in pyridine followed by treatment of the product with caustic soda or directly in the presence of the alkali. They have recently been obtained by treating dextran with a mixture of polyphosphoric acid and a trialkylamine[162]. Dextran phosphates form complexes with lipoproteins[163], and can

be used to obtain polymeric medicinals and photographic materials[164].

Studies have been made on the effect of the reaction conditions on the composition of nitric esters formed by the nitration of dextran with concentrated nitric acid and various nitrating mixtures[55,165-167]. Nitration with a mixture of 64% of nitric acid, 26% of orthophosphoric acid, and 10% of phosphorus pentoxide produces no decreases in the degree of polymerisation of dextran[168]. Highly substituted dextran nitrates are soluble in acetone, dimethylformamide, cyclohexanone, and oxolan. The infrared spectra over the range 700–1000 cm^{-1} indicate that the monomer units of dextran nitrate macromolecules have the same conformation ($C1$) as those of dextran itself[55,167]. Dextran trinitrate is an amorphous polymer[55], which absorbs water vapour[54]. Dextran xanthates have been obtained[169] and proposed for use in fibre production and the finishing of paper and textiles. Dextran methyl xanthate has been prepared and subjected to pyrolysis at 160°C.[170]

Esters with Organic Acids

Detailed investigations on the acetylation of dextran with various acetylating mixtures have yielded dextran acetates having degrees of substitution up to 3.0[55,167,171-173]. The rate of acetylation depends significantly on the conditions of preliminary activation of the dextran: a sharp increase in rate was observed after preliminary activation by reprecipitation from water into glacial acetic acid[55,167]. The infrared spectrum over the range 1270–1420 cm^{-1} of dextran activated in this way differs markedly from those of non-activated dextran and of dextran activated by treatment with glacial acetic acid[55,167].

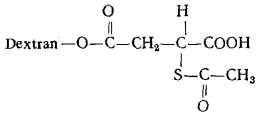
Investigation of the distribution of substituents in partly substituted dextran acetates has shown that acetylation of dextran with acetic anhydride in the presence of sodium acetate gives a product in which the 2-, 3-, and 4-hydroxyls are approximately equally reactive, whereas the 2-hydroxy-groups are most reactive in the product obtained with acetic anhydride in an equimolecular mixture of formamide and pyridine[172]. Since the infrared spectrum of dextran triacetate at 700–1000 cm^{-1} is identical with that of dextran, the monomer units in the corresponding macromolecules can be assumed to have the same conformation ($C1$). Only one solvent—symmetrical tetrachloroethane—is at present known for the triacetates of various dextran preparations[167,171,173,174]. The formula $[\eta] = 10^{-3}M^{0.5}$ has been proposed[171] for the viscosimetric determination of the molecular weight of dextran triacetate in this solvent.

Thermomechanical examination and X-ray diffraction indicate that dextran triacetate is a crystalline polymer (melting point 210°C).[55] The crystalline structure was improved by heating in tetrachloroethane and evaporating off the solvent. The heats of interaction of dextran triacetate with water and with dimethylformamide are respectively 3.0 and −9.4 cal g^{-1}, while the "water surface" calculated from the water-vapour sorption isotherm is 45 $m^2 g^{-1}$.[54]

Esters of dextran with aromatic carboxylic acids (benzoic, acetylsalicylic, cinnamic, nitrobenzoic) have been prepared by treating the polysaccharide with the acid chlorides in absolute pyridine[175] and by nucleophilic substitution of dextran nitrate by the action of the sodium salts in aqueous dimethylformamide[176]. The latter reaction has an S_N2 mechanism. Dextran phenyl diphenylcarbamate is obtained by the action of phenyl isocyanate on dextran[177]. The succinate, maleate, and phthalate, which are able to form complexes, have been obtained by the action of the acid anhydrides in formamide and pyridine[178,179]. Treatment of dextran maleate with sodium hydrogen sulphite yields an ester containing both carboxylate and sulphonate groups:

$$\text{Dextran}\!-\!OCOCH\!=\!CH\!-\!COOH + NaHSO_3 \rightarrow \text{Dextran}\!-\!OCOCH_2\!-\!\underset{\displaystyle SO_3Na}{\underset{|}{CH}}\!-\!COOH .$$

Dextran reacts with S-acetylthiosuccinic anhydride to give the corresponding ester[180]:

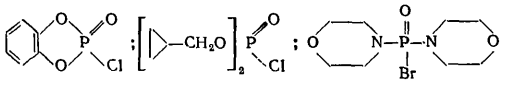


A systematic investigation has been made of the preparation of dextran esters of N-substituted α-amino-acids and the possibility of obtaining from them derivatives of dextran containing a free amino-group[181-188]. The esters were obtained by the action of the acids in the presence of NN'-dicyclohexylcarbodi-imide[181,182] by a method providing for the formation of mixed anhydrides[183-185] (these are formed when the amino-acids are treated with ethyl chloroformate, phosphoryl chloride, toluene-p-sulphonyl chloride, or benzenesulphonyl chloride in the presence of an organic base), by treating dextran with imidazolides of N-protonated α-amino-acids (obtained by the reaction of trifluoroacetates or hydrochlorides of the α-amino-acids with thionyl- or carbonyl-bi-imidazolyl)[186,187], and also by transesterification of p-nitrophenyl esters of the N-substituted α-amino-acids with dextran in dimethyl sulphoxide in the presence of excess of imidazole[188].

Of the various groups used to protect the amino-group in the acids nitrophenylsulphonyl is the most easily removed, by treatment with thiophenol in a mixture of dimethyl sulphoxide and pyridine or in the sodium thiosulphate–potassium iodide system in aqueous solution[183]. When dextran is treated with N-protonated imidazolides of α-amino-acids, poly(amino-acid) residues are added to the macromolecule[186]. Adenine, thymine, and uracil residues are introduced into the macromolecule by treating dextran with the carboxymethylated bases in the presence of dicyclohexylcarbodi-imide[189]; the resulting dextran esters form compounds with polynucleotides.

Toluene-p-sulphonic and methanesulphonic esters of various polysaccharides are widely used as intermediates for preparing derivatives of the polysaccharides by nucleophilic substitution. Considerable interest therefore attaches to the recent preparation of the dextran esters from the acid chlorides[115,190]. A similar scheme has been used to prepare the 5-dimethylaminonaphthalene-1-sulphonic ester (which is fluorescent)[191] and the p-iodobenzenesulphonic ester[192]. The latter has been proposed for preparing tissues of various animal organs for electron microscopy.

Phosphorus-containing esters can be obtained[193] by treating dextran with compounds of the type



A compound which may be used to detect specific immunoglobulin receptors on the surface of tumour cells is obtained by the action of fluorescein isothiocyanate on dextran[194]. A water-soluble ester is obtained from dextran and a chlorotriazine reactive blue dye (Dextran Blue

2000), which can be used to determine the dead space in column gel permeation, to check that the column is correctly packed, and as substrate in estimating the activity of enzymes that hydrolyse dextran[195-202]. Dextran coloured with a reactive orange dye has been suggested for use in thin-layer gel permeation[203,204].

VII. DEXTRAN ETHERS

The main lines of development at present are the preparation of ethers containing various reactive functional groups, elaboration of new methods for preparing already known ethers, determination of the distribution of alkyl groups at carbon atoms in the anhydro-D-glucopyranose unit, and study of the properties and possible fields of application of dextran ethers.

The completely substituted methyl ether of dextran had been obtained earlier by repeatedly treating sodium dextranate with methyl iodide or dextran with dimethyl sulphate or methyl iodide in the presence of alkali. This ether has now been obtained[205] by treating dextran acetate, which is soluble in acetone, first with dimethyl sulphate and then with methyl iodide in the presence of silver oxide. A single-stage preparation of the completely substituted methyl ether involves treating dextran in dimethyl sulphoxide with methyl iodide in the presence of the methylsulphonylmethyl carbanion in an atmosphere of nitrogen[206].

In the methylation of dextran with dimethyl sulphate in a homogeneous medium the relative rate constants for the hydroxyls at positions 2–4 are 8 : 1 : 3.5.[207] The probable reason is that the 2-hydroxyl, in the α-position to the glycosidic link and arranged equatorially in the monomer unit of dextran, is more acidic than the hydroxyls at positions 3 and 4. The 3-hydroxyl shows the lowest reactivity also in the methylation of dextran with methyl iodide[55]. Infrared spectra have been published for methyl ethers of dextran of different degrees of substitution[167]. An ethyl ether has been obtained by treating dextran dissolved in 10% caustic soda with ethyl bromide[55,167].

Dextran ethers containing hydroxyalkyl groups—2-hydroxyethyl, 2-hydroxypropyl, 2-hydroxybutyl—can be obtained, according to the patent literature, by the action of compounds containing α-oxide rings or 1,2-halogenohydrin groups on dextran in alkaline medium. Reaction between dextran and epoxides may yield not only the ether but also graft copolymers by interaction of the epoxides with the hydroxy-groups in the alkyls:

$$\text{Dextran}-O-CH_2-CH_2OH + n\,CH_2-CH_2 \rightarrow \text{Dextran}-O(CH_2CH_2O)_n-CH_2CH_2OH\ .$$

The distribution of alkyl groups in a 2-hydroxyethyl ether obtained by the action of oxiran on dextran dissolved in 0.25% caustic soda has recently been examined[208]. Analysis by gas–liquid chromatography with reference samples of the products of the acid hydrolysis of the ether shows that the alkyls are distributed among positions 2–4 in the proportions 5.8 : 1 : 3.

Preparation of the water-soluble 3-chloro-2-hydroxypropyl ether by treating dextran with epichlorohydrin in the presence of zinc tetrafluoroborate[209]

$$\text{Dextran}-OH + CH_2-CH-CH_2Cl \xrightarrow{Zn(BF_4)_2} \text{Dextran}-O-CH_2-CH(OH)-CH_2Cl$$

is of considerable interest as a method of introducing reactive chlorohydrin groups into the macromolecule. This ether is the starting material for the preparation of other dextran ethers[210-212] and polymeric medicinals[115,119,121,123,124]. A dextran derivative labelled with radioactive iodine can be obtained by first treating dextran with allyl bromide and then iodinating the resulting allyl ether with radioactive iodine[213,214].

Cyanoethyl and carbamoylethyl ethers of various degrees of substitution have been prepared by nucleophilic addition to dextran of acrylonitrile and acrylamide in the presence of caustic soda[167,168,210,211,215]:

$$\text{Dextran}-OH + CH_2=CH-CN \rightarrow \text{Dextran}-O-CH_2-CH_2-CN$$

$$\text{Dextran}-OH + CH_2=CH-C(=O)-NH_2 \rightarrow \text{Dextran}-O-CH_2-CH_2-C(=O)-NH_2\ .$$

Investigation of cyanoethyl ethers of low degrees of substitution has established that cyanoethylation of one of the secondary hydroxyls in a monomer unit of dextran diminishes the rate of cyanoethylation of the other secondary hydroxyls in that unit[55,167]. In the initial stage acrylonitrile reacts mainly with the 2- and 4-hydroxyls[55]. A cyanoethyl ether of degree of substitution 3.0 is crystalline (melting point 80°C)[55], and its crystal structure is improved by heating it in dimethylformamide and then evaporating off the solvent. Data have been published on the sorption of water vapour and the heats of interaction with water and with dimethylformamide for this ether[54], and infrared spectra for cyanoethyl ethers of dextran having various degrees of substitution[167,216].

A trityl ether can be prepared[168,217] by treating dextran with chlorotriphenylmethane in the presence of pyridine:

$$\text{Dextran}-OH + ClC(C_6H_5)_3 \rightarrow \text{Dextran}-O-C(C_6H_5)_3\ .$$

An ether has been prepared also with oxan-2-ol[218]. The addition of D-mannose and D-xylose to dextran has been reported[219].

Dextran Ethers containing Ionogenic, Complexing, or Electron-exchange Groups

Increasing interest has been taken during recent years in the preparation, properties, and fields of application of dextran ethers containing ionogenic, complexing, or electron-exchange groups. A considerable number of scientific papers and patents have been published on the preparation and application of the carboxymethyl ether[220-222], obtained by treating dextran with sodium chloroacetate in the presence of caustic soda:

$$\text{Dextran}-OH + ClCH_2COONa \xrightarrow{NaOH} \text{Dextran}-OCH_2COONa\ .$$

The patent literature describes the application in veterinary practice of compounds (probably complex) formed in an alkaline medium between dextran carboxymethyl ether and iron hydroxide (for the treatment of anaemia), as well as cobalt and copper hydroxides. The product obtained from the ether with a basic aluminium salt has been proposed for the treatment of ulcers. The ether can be used also for the preparation of polymeric medicinals[115,119,120,123,124], the production of long acting forms of medicines (tablets), X-ray contrast media, cosmetic preparations, paints and varnishes, and in the foodstuffs industry[9,223,224]. Various methods for preparing derivatives of dextran carboxymethyl ether containing α-amino-acid residues have been studied in detail[225-228].

In the presence of caustic soda dextran reacts with the sultone of 3-hydroxypropanesulphonic acid, chloromethylphosphonic acid, and thi-iran to give the water-soluble

sulphopropyl, dihydroxyphosphinylmethyl, and mercaptoethyl ethers[209,210,229]:

$$\text{Dextran}-OCH_2CH_2CH_2SO_3Na, \quad \text{Dextran}-OCH_2PO(ONa)_2,$$
$$\text{Dextran}-OCH_2CH_2-SNa$$

The first of these ethers is a strong polyelectrolyte; the second and third ethers possess respectively complexing and electron-exchange properties. The infrared spectra have been published[230]. The sulphopropyl ether exhibits anticoagulant activity, and has been used to obtain polymeric medicinals[115,119-124,231].

Several new water-soluble dextran derivatives containing various ionogenic, complexing, and electron-exchange groups have been prepared[115,121,168,210-212,232] by the action on the 3-chloro-2-hydroxypropyl ether of ammonia, aliphatic amines, aliphatic and aromatic amino-carboxylic acids, hydrazine, sodium sulphide, and other compounds according to the general scheme

$$\text{Dextran}-OCH_2-\underset{\underset{OH}{|}}{CH}-CH_2Cl \xrightarrow{HX} \text{Dextran}-OCH_2-\underset{\underset{OH}{|}}{CH}-CH_2X + HCl$$

where X is a molecular residue of one of the above monomeric agents. Water-soluble dextran ethers containing thiocarbamoyl and amidrazone groups, which possess complexing properties, have been prepared[168,213] from the cyanoethyl ether:

$$\text{Dextran}-OCH_2-CH_2CN \xrightarrow{H_2S} \text{Dextran}-OCH_2-CH_2C(=NH)SH$$
$$\text{Dextran}-OCH_2-CH_2CN \xrightarrow{H_2NNH_2} \text{Dextran}-OCH_2-CH_2C(=NH)NH-NH_2 .$$

The infrared spectra of these ethers have been published[219]. The above dextran derivatives, containing various complexing groups and prepared from the 3-chloro-2-hydroxypropyl and cyanoethyl ethers, form water-soluble complexes with several bivalent metals—copper, cobalt, nickel, and mercury—whose stability constants have been given in Ref. 168.

Treatment of dextran in alkaline medium with 1-diethylamino-2,3-epoxypropane and 1-chloro-2-diethylaminoethane yields[233,234] the 3-diethylamino-2-hydroxypropyl and diethylaminoethyl ethers

$$\text{Dextran}-O-CH_2-\underset{\underset{OH}{|}}{CH}-CH_2-N(C_2H_5)_2, \quad \text{Dextran}-O-CH_2CH_2-N(C_2H_5)_2 .$$

The diethylaminoethyl ether has been quaternised with benzyl chloride[235]. Dextran ethers containing primary and tertiary aliphatic amino-groups have been investigated by potentiometric titration[121,236-238]. Viscosity measurements on solutions of carboxymethyl, diethylaminoethyl, and quaternised diethylaminoethyl ethers of dextran at various ionic strengths[137] suggest that the ether macromolecules are very flexible. A water-soluble ether containing aromatic amino-groups has been prepared[210] by treating dextran in alkaline medium with the sulphuric ester of 2-(3-amino-4-methoxyphenylsulphonyl)ethanol:

$$\text{Dextran}-OH + NaO_3SOCH_2-CH_2-O_2S-C_6H_3(NH_2)(OCH_3) \xrightarrow{Na_2CO_3}$$
$$\rightarrow \text{Dextran}-OH + CH_2=CH-SO_2-C_6H_3(NH_2)(OCH_3) \xrightarrow{NaOH}$$
$$\rightarrow \text{Dextran}-OCH_2CH_2SO_2-C_6H_3(NH_2)(OCH_3) .$$

The resulting 2-(3-amino-4-methoxyphenylsulphonyl)ethyl ether was used for the preparation of graft copolymers of dextran[214,239,240]. Dextran reacts also with chlorotrialkyl(aryl)silanes and hexa-alkyldisilazanes[241].

Several workers have shown that the diethylaminoethyl ether of dextran enhances interferon formation and antiviral activity caused by the introduction of polynucleotides into animals or into a cellular culture[242-244]. Pretreatment of the cells (before introduction of polynucleotides) with the diethylaminoethyl ether also increases viral resistance. The 3-diethylamino-2-hydroxypropyl ether of dextran possesses similar properties[245]. Nevertheless, the diethylaminoethyl ether increases the infective activity of viruses[246-249]. The reasons for these phenomena are firstly that this dextran ether protects nucleic acids and polynucleotides (by forming compounds with them) from the degrading action of nucleases and secondly that it promotes penetration of polynucleotides and nucleic acids into the cells by reacting with the cell membrane[242,246,248-250]. However, it has been stated[251,252] that dextran diethylaminoethyl ether is also able to suppress the growth of viruses.

VIII. DERIVATIVES WITH A THREE-DIMENSIONAL CROSS-LINKED STRUCTURE

Derivatives of dextran having a three-dimensional cross-linked structure, known under the general name Sephadexes, are obtained by treatment with epichlorohydrin in an alkaline medium[253-256]. Intermolecular bonds are formed by the reactions

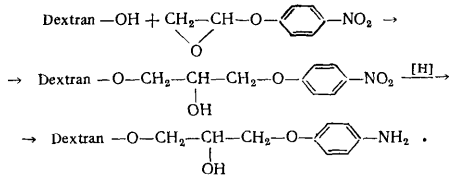
$$\text{Dextran}-OH + CH_2-\underset{\underset{O}{\diagdown\diagup}}{CH}-CH_2-Cl \xrightarrow{NaOH}$$
$$\rightarrow \text{Dextran}-O-CH_2-\underset{\underset{OH}{|}}{CH}-CH_2-O-\text{Dextran} .$$

Sephadexes of different degrees of cross-linking, differing in gel pore size and in ability to swell in water, are obtained by varying the reactant concentrations and also the molecular weight of the dextran. Several brands of Sephadex G are marketed at the present time, and are widely used in gel permeation in aqueous media for preparative and analytical purposes[257-260]. Other cross-linking agents suitable for application to dextran are glycidyl tetramethylene ether[261] and 1,2 : 3,4-diepoxybutane[256]. Cross-linked dextran derivatives can be used in perfumery and cosmetics[262].

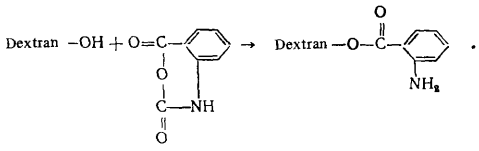
Alkylation or acylation of the hydroxy-groups of the dextran macromolecules in Sephadexes yields derivatives which swell well in organic solvents while retaining the ability to fractionate substances according to molecular dimensions. The hydroxyls of the dextran can be blocked by subjecting Sephadexes to acetylation[263,264], benzoylation[265], methylation[266], or treatment with aliphatic isocyanates[267] or aliphatic α-oxides[268]. Thus Sephadex LH-20 is Sephadex G-25 treated with an aliphatic epoxide.

Cross-linked dextran derivatives have been obtained containing aminoethyl[269], sulphoethyl[270] and sulphopropyl, carboxymethyl[270,271], diethylaminoethyl[270,272], and quaternary ammonium groups[273]; the last four are marketed under the respective names SP, CM, DEAE, and QAE Sephadexes[274]. These Sephadexes possess ion-exchange properties and are widely used for the separation of biologically active substances such as proteins, hormones, nucleic acids, etc.

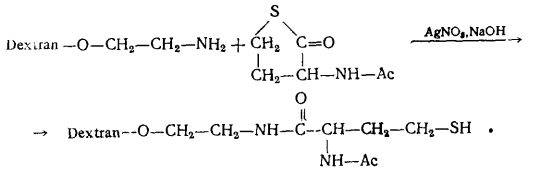
Cross-linked dextran ethers containing aromatic amino-groups have been prepared in three ways. Firstly, treatment of a cross-linked dextran derivative with 1,2-epoxy-1-*p*-nitrophenoxypropane is followed by reduction of the nitro-groups to amino[275,276]:



The second method consists in reaction between a cross-linked dextran derivative and the sulphuric ester of 2-(3-amino-4-methoxyphenylsulphonyl)ethanol[277]. Thirdly, carbon dioxide is evolved when dextran is treated with *N*-carboxyanthranilic anhydride[278]:



A derivative containing isothiocyanato-groups was obtained by treating a cross-linked 3-*p*-aminophenoxy-2-hydroxypropyl ether of dextran with thiocarbonyl chloride[275]. These polymers, containing isothiocyanato- or aromatic amino-groups, are used to prepare insoluble derivatives of enzymes and antibodies. A cross-linked dextran derivative containing mercapto-groups was prepared[269] by the reactions



This polymer can be used to prevent the oxidation of compounds containing thiol groups[279,280].

A cross-linked dextran derivative containing an organomercury residue (which can be used to isolate proteins containing thiol groups) has been obtained[281] by alkylating dextran with 1-allyloxy-2,3-epoxypropane and then treating with mercury acetate. Patents and scientific papers[282-284] have reported the preparation of cross-linked dextran derivatives possessing complexing properties. An insoluble cross-linked dextran derivative coloured with a reactive dye can be used as substrate in studying the activity of enzymes that hydrolyse dextran[261]. The rate of oxidation of Sephadexes by periodic acid is not much lower than the rate of oxidation of dextran in solution[285].

IX. PREPARATION OF GRAFT COPOLYMERS OF DEXTRAN

Graft copolymers of dextran have been obtained with carbon-chain polymers, starch, polypeptides, and biologically active proteins (enzymes, antigens, and hormones). Detailed investigations of the preparation of graft copolymers with polyacrylic acid and with poly-2-methyl-5-vinylpyridine used as initiators redox systems in which the oxidants were cerium(IV) or vanadium(V) compounds and the reductants respectively dextran or its 2-(3-amino-4-methoxyphenylsulphonyl)ethyl ether[214,239,240]. These methods of preparation enabled the length of the grafted chain to be controlled, and water-soluble graft copolymers of dextran with polyacrylic acid or with poly-2-methyl-5-vinylpyridine containing up to 30–40% of the grafted polymer to be obtained without accompanying formation of a carbon-chain homopolymer.

These methods are characterised by high reaction velocities, the formation of comparatively short grafted chains, and a high degree of involvement of macromolecules of the 2-(3-amino-4-methoxyphenylsulphonyl)ethyl ether of dextran (up to 70% in the grafting of polyacrylic acid), which are explained by the occurrence of copolymerisation in a homogeneous medium. Cerium(IV) compounds have been used to initiate the graft copolymerisation of comparatively short polyacrylamide chains with dextran[286]. A graft copolymer of dextran and poly(methyl methacrylate) has recently been synthesised by anionic polymerisation involving treatment of a dextranate with methyl methacrylate in the presence of dimethyl sulphoxide[287]. A graft copolymer of dextran and polytyrosine is obtained by treating the aminoethyl ether of dextran with the anhydride of *N*-carboxy-L-tyrosine[288]. Graft copolymers of dextran and polypeptides have been obtained also by treating sodium dextranate with anhydrides of other *N*-carboxy-*α*-amino-acids[184], by reaction between the carboxymethyl ether of dextran and a peptide in the presence of dicyclohexylcarbodi-imide, and by acylating dextran with a succinyloligopeptide in the presence of dicyclohexylcarbodi-imide[289].

The starting material in the preparation of a graft copolymer with starch is a cyclic carbonate obtained by treating dextran with chloroform, whose ester groups react with starch[290]. The addition of insulin to dextran pretreated with cyanogen bromide is of great interest[291,292]. The activity of the relatively non-toxic water-soluble product is closely similar to that of the original insulin both *in vitro* and *in vivo*; its immunochemical activity is less than that of free insulin, but the lipoglycaemic action is stronger and more prolonged. A graft copolymer of dextran and insulin (when injected in smaller doses than the original insulin) induced the formation of several enzymes in the liver of animals suffering from diabetes. Yet other workers state[293] that the biological activity of the insulin derivative obtained in this way is considerably below that of the initial insulin.

During recent years increasing interest has been aroused by the preparation of insoluble derivatives of biologically active proteins (enzymes, antigens, antibodies), which can be used as specific catalysts, immunosorbents, or sorbents for affinity chromatography[294-298]. Starting materials used for the addition of enzymes have been cross-linked dextran derivatives containing carboxyl[299], diethylaminoethyl[300,301], or isothiocyanate[275,276] groups or aromatic amino-groups[302,303], as well as Sephadexes treated with phenyl isocyanate[304] or cyanogen bromide[305-310]. In these insoluble derivatives the enzyme macromolecules are attached to the dextran macromolecules by ionic[300,301] or covalent[275,276,302-310] bonds.

Interesting results have been obtained[309] showing that the activity of trypsin added to Sephadex pretreated with cyanogen bromide is 15–35% of that of the original enzyme; but if the dextran in this compound is subjected to enzymic hydrolysis with dextran glucosidase, the activity of the resulting water-soluble trypsin derivative is 60–100% of the original. This technique can probably be widely used

in the future to analyse the reasons for the decrease in activity of enzymes attached to insoluble dextran derivatives. A graft copolymer of cross-linked dextran and trypsin can be used[310] to isolate the ovomucoid glycoprotein by affinity chromatography. The properties of nucleases can be improved by addition to soluble dextran derivatives[311].

Table 1. Reactions used to obtain medicinal polymers based on dextran and its derivatives. (D = dextran macromolecule; M = residue of medicinal molecule; DCCD = dicyclohexyldi-imide).

1. $D{-}OH + C(=O)(OH){-}M \rightarrow D{-}O{-}C(=O){-}M$[121,322];

2. $D{-}OH + Cl{-}C(=O){-}M \rightarrow D{-}O{-}C(=O){-}M$[9,175,323,324];

3. $D{-}OH + HOOC{-}M \xrightarrow{DCCD} D{-}O{-}C(=O){-}M$[289];

4. $D{-}COOH + H_2N{-}M \rightarrow D{-}COO^{-}(H_3\overset{+}{N}{-}M)$[116,121];

5. $D{-}OSO_3Na + HCl \cdot H_2N{-}M \rightarrow D{-}OSO_3^{-}(H_3\overset{+}{N}{-}M)$[160,325–328];

6. $D{-}OCH_2CH_2CH_2SO_3H + H_2N{-}M - D{-}OCH_2CH_2CH_2SO_3^{-}(H_3\overset{+}{N}{-}M)$[115,119–121,123,124,231];

7.* $D{-}O{-}CH_2CH_2SO_3H + H_2N{-}M \rightarrow D{-}O{-}CH_2CH_2SO_3^{-}(H_3\overset{+}{N}{-}M)$[329];

8. $D{-}OCH_2COOH + H_2N{-}M \rightarrow D{-}O{-}CH_2COO^{-}(H_3\overset{+}{N}{-}M)$[115,119–121,123,124];

9. $D{-}O{-}CH_2{-}CH(OH){-}CH_2{-}\overset{+}{N}(C_2H_5)_3 + HOOC{-}M \rightarrow$

$\rightarrow D{-}O{-}CH_2{-}CH(OH){-}CH_2{-}\overset{+}{N}(C_2H_5)_2(\bar{O}\bar{O}C{-}M)$[115,123,124];

10*. $D{-}O{-}CH_2CH_2{-}N(C_2H_5)_2 + HO_3S{-}M \rightarrow$

$\rightarrow D{-}O{-}CH_2{-}CH_2{-}\overset{+}{N}(C_2H_5)_2(O_3\bar{S}{-}M)$[330];

11. $D{-}O{-}CH_2{-}C(=O){-}O{-}C(=O){-}O{-}C_2H_5 + H_2N{-}M \rightarrow D{-}O{-}CH_2{-}C(=O){-}NH{-}M$[120,121]

12. $D{-}O{-}CH_2{-}COOH + H_2N{-}M \xrightarrow{DCCD} D{-}O{-}CH_2{-}C(=O){-}NH{-}M$[288];

13. $D{-}O{-}CH_2{-}CH(OH){-}CH_2Cl + H_2N{-}M \rightarrow D{-}OCH_2{-}CH(OH){-}CH_2{-}NH{-}M$[115,119,121,123,124]

14. $D{-}O{-}CH_2{-}CH(OH){-}CH_2{-}NH{-}C_2H_4{-}OH + H_2CO + H_2N{-}C(=O){-}M \rightarrow$

$\rightarrow D{-}O{-}CH_2{-}CH(OH){-}CH_2{-}N(CH_2{-}NH{-}C(=O){-}M){-}C_2H_4OH$[115,123,124];

15. $D{-}Cl + H_2N{-}M \rightarrow D{-}NH{-}M$[115];

16. $D{-}NH_2 + H_2CO + H_2N{-}C(=O){-}M \rightarrow D{-}NH{-}CH_2{-}NH{-}C(=O){-}M$[218];

17. $D{-}C(H)=O + H_2N{-}M \rightarrow D{-}C(H)=N{-}M$[115,118–124,231,232];

18. $D{>}C=O + H_2N{-}M \rightarrow D{>}C=N{-}M$[115];

19. $D{-}OR{-}C_6H_4{-}CH(=O) + H_2N{-}M \rightarrow D{-}O{-}R{-}C_6H_4{-}CH=N{-}M$[116].

* Dextran derivatives having a three-dimensional cross-linked structure are used in reactions 7 and 10.

When an animal is immunised by the hypodermic, intramuscular, or intraperitoneal injection of an insoluble graft copolymer of cross-linked dextran and an antigen, the synthesis of antibodies in the organism lasts longer than on immunisation with a soluble antigen[312,313]. A repeat immunisation with a soluble antigen of an animal previously injected with the above graft copolymer caused extraordinarily intense production of antibodies, in numbers exceeding by factors of 10–20 those formed if the first immunisation had been made with a soluble antigen. This work established that the injected insoluble graft copolymer of dextran and antigen is gradually absorbed, probably by the action of dextran glucosidase present in the animal organism.

X. DERIVATIVES CONTAINING ATTACHED MEDICINALS

During the past decade the achievements of the chemistry of macromolecular compounds have been used ever more frequently and widely in the solution of medical problems[314–321]. An urgent line of research is the synthesis of polymeric medicinals by attaching drugs of low molecular weight to water-soluble or -insoluble polymers.

Table 2. Brief summary of effects achieved by the attachment of medicinals of low molecular weight to dextran.

Reaction	Dextran derivative	Medicinal	Effect	Ref.
1	Dextran	pelentan	water solubility	121, 322
2	Dextran	aspirin	less toxic	175
2	Dextran	nicotinic acid	prolongation	9
3	Dextran	oligopeptide analogue of eledoisin	prolongation	289
5	Sulphate	streptomycin, neomycin	prolongation, increased concn. in lymphatic system	160, 325
5	Sulphate	mitomycin	increased antitumour activity	326
6	Sulphopropyl ether	cystamine	prolongation, more effective	121, 231
7	Cross-linked sulphoethyl ether	papaverine, codeine	better taste, less toxic	329
8	Carboxymethyl ether	Tubazid	prolongation	119, 121
8	Carboxymethyl ether	kanamycin	prolongation	115
11	Carboxymethyl ether	serotonin	less toxic	120, 121
12	Carboxymethyl ether	peptide analogue of eledoisin	prolongation	289
17	Dialdehydo	kanamycin	prolongation	115
17	Dialdehydo	Tubazid	prolongation, less toxic	119, 121, 122
17	Dialdehydo	serotonin	prolongation, less toxic	120, 121
17	Dialdehydo	4-methylthiosemi-carbazide	antitumour activity	331
17*	Dextran	tetracycline	prolongation	333, 334
17*	Dextran	thyrocalcitoin hormone	prolongation	335

* Probably complex compounds.

The purpose is to improve the properties of the drugs—to prolong their action and enhance their activity, lower the toxicity, change the distribution in the organism, improve solubility, and increase stability to the action of enzyme systems in the organism that tend to destroy them.

In the preparation of polymeric medicinals for introduction into the organism, especially by injection, it is necessary to take into account the ability of the polymer to be assimilated in the organism and to be isolated from

the latter after fulfilling its functions. From this point of view the use of dextran for the production of physiologically active polymers is of considerable interest, as it is gradually hydrolysed by enzymes in the organism, which eliminates the danger of accumulation of the polymer in the tissues of various organs. The gradual enzymic cleavage of dextran in the organism may not permit the action of drugs to be prolonged to the extent achieved by the use of synthetic carbon-chain polymers, which are not broken down in the organism, but in many cases this is not required: it is sufficient to increase the period of action of the medicinals to a few hours or days. Table 1 lists the reactions used to obtain medicinal polymers based on dextran. Table 2 summarises the information in the scientific literature on the effects achieved by the chemical attachment of drugs of low molecular weight to derivatives of dextran.

Several workers have shown that the nature of the chemical bond between the dextran derivative and the attached medicinal has a significant influence on the biological properties of the resulting medicinal polymer, e.g. on the antibacterial activity of polymeric derivatives of isonicotinohydrazide[119,121] and antibiotics (kanamycin, ampicillin, tetracyclines)[115,123,124], and on the toxicity of polymeric derivatives of serotonin[120,121]. Available experimental results show that attachment to dextran and its derivatives can be regarded as a method for improving the properties of medicinal drugs.

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Mass Spectrometry of Chromen-2-ones (Coumarins) and of Furo- and Pyrano-chromenones

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Mass-spectrometric results for the coumarins, furocoumarins, and pyranocoumarins are summarised. The characteristic elimination of carbonyl groups characteristic of coumarin itself can be traced also in the spectra of substituted (halogenated, hydroxylated, methoxylated, carbonylated, *O*- and *C*-alkylated, and *O*- and *C*-acylated) coumarins, but the nature of the substituent has a decisive influence on the way in which derivatives break down, and in many cases elimination of carbonyl groups takes place only after partial or complete elimination of the substituent. With bicoumarins elimination of carbonyl groups is observed in the later stages of decomposition or not at all. The regularities reported for coumarins are found also with furo- and pyrano-coumarins. Differences in the spectra of positional isomers are usually apparent only in differences in the peak intensities of the characteristic ions. There is a list of 59 references.

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I. INTRODUCTION

We began the mass-spectrometric investigation of natural chromen-2-ones (coumarin, umbelliferone, herniarin, and osthol) in 1963.[1] Independently, but a little later (1964), the same chromenones were studied by Barnes and Occolowitz[2]. The largely identical results obtained in the two investigations showed that, because of the specificity of the breakdown of chromen-2-ones on electron bombardment and the characteristic influence of the number, nature, and position of substituents on this process, mass spectrometry is an extremely promising method in this case as with other classes of naturally occurring compounds. This promise has been fully confirmed by the further accumulation of experimental information. The number of mass-spectrometric investigations on chromenones and their derivatives, including furo- and pyrano-chromenones, has now become very considerable, which has led us to attempt in this Review to systematise and summarise the accumulated results.

II. CHROMEN-2-ONE AND ITS HALOGENO-DERIVATIVES

The spectrum of chromen-2-one itself (I) is very simple (Fig. 1*a*), containing only five peaks—one due to the molecular ion having $m/e = 146$, peaks due to the repeated elimination of 28 amu (atomic mass units) ($m/e = 118$ and 90) and the loss of 29 amu at the second stage (or the detachment of 1 amu after the second elimination of 28 amu) ($m/e = 89$), and a fifth peak with $m/e = 63$, caused by breakdown of the aromatic ring and devoid of diagnostic significance.

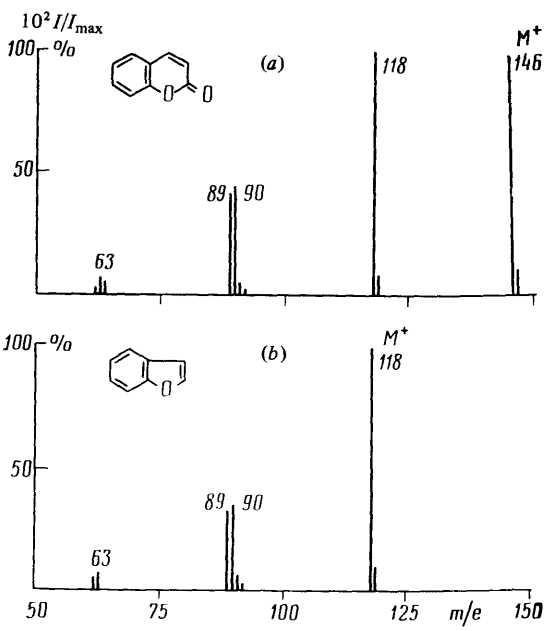


Figure 1. Mass spectra of: *a*) chromen-2-one; *b*) benzofuran.

It was reasonable to suppose that the first stage of decomposition involved elimination of the lactonic carbonyl, although the possibility of elimination of an ethylene molecule involving the 3- and 4-carbon atoms with migration

of two hydrogen atoms from the charged fragment could not be completely excluded. The first hypothesis is unambiguously supported by Zakharov's observations[3] of shifts of 1 amu to 119 and 91 (m/e) respectively in the peaks due to the ions $[M - 28]^+$ and $[M - 2 \times 28]^+$ in the mass spectra of the 3- and 4- deutero-analogues of chromen-2-one (Table 1). Similarly, double elimination of 28 amu occurs in the spectra of 3-chloro-, 4-chloro-, and 3,4-dichlorochromen-2-ones. Only in the spectrum of 3-bromochromen-2-one is this sequence changed: a molecule of carbon monoxide is eliminated first, then the bromine atom, and after this another carbon monoxide molecule.

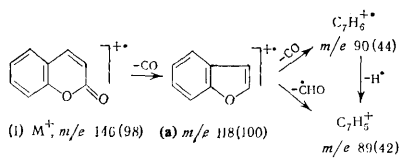
Table 1. Peaks (m/e) of main ions in the mass spectra of chromen-2-one and its deutero- and halogeno-derivatives (values of $100I/I_{max}$ given in parentheses, where I_{max} is the maximum intensity in the spectrum).

Chromenone derivative	M+	M—CO	M—2CO	M—Hal	M—Hal—CO	M—2CO—Hal
Chromen-2-one (I)	146 (98)	118 (100)	90 (44)	—	—	—
3-Deutero	147 (86)	119 (100)	91 (75)	—	—	—
4-Deutero	147 (88)	119 (100)	91 (41)	—	—	—
3-Chloro	180 (75) / 182	152 (43) / 154	124 (18) / 126	145 (8)	117 (6)	89 (100)
4-Chloro	180 (99) / 182	152 (44) / 154	124 (15) / 126	145 (10)	117 (10)	89 (100)
3,4-Dichloro	214 (83) / 216	186 (47) / 188	158 (23) / 160	—	—	123 (100) / 125
3-Bromo	224 (74) / 226	196 (22) / 198	—	145 (40)	117 (8)	89 (100)

A second mode of decomposition is also evident in the spectra of all the halogenated chromen-2-ones: elimination of the halogen atom from the molecular ion is followed by double elimination of carbonyl (Table 1).

In order to ascertain the possible structure of the $[M - CO]^+$ ion both the Reviewers[1] and the Australian workers[2] compared the mass spectra of chromen-2-one and benzofuran (*a* and *b* in Fig. 1), and concluded from their identity, beginning with the 118 peak ($[M - 28]^+$ for chromenone and the peak due to the molecular ion of benzofuran), that the molecular ion of chromenone, on losing a carbonyl group, is converted into a benzofuran ion (a), which in turn loses the second carbonyl group and then a hydrogen atom or else a formyl group at once (Scheme 1).

Scheme 1



The structure of the 118 ion has since been discussed many times, with arguments both for[4] and against[5-8] the benzofuran structure. The latter view was based on the difference between the appearance potential of the 118 ion on breakdown of the molecular ion of chromenone and the ionisation potential of benzofuran. In the Reviewers' opinion a more convincing argument is the similarity in the spectra of these two compounds, not only in the m/e values but also in the intensities of corresponding peaks (*a* and *b* in Fig. 1). However, this question has not been finally settled.

The spectrum of the corresponding dihydro-derivative—chroman-2-one, melilitol (II)—is very similar to that of the chromenone[2]: it too is characterised by successive double elimination of 28 amu with subsequent loss of a hydrogen atom (or elimination of 29 amu together at the second stage). In this case, however, elimination of an ethylene molecule instead of a carbonyl group is more probable at the first stage, since with (II) this process does not require the migration of two hydrogen atoms from the charged fragment.

The mass spectra of substituted chromenones reflect their specific characteristics resulting from the nature, number, and positions of substituents, as has already been partly shown by the halogeno-derivatives.

III. HYDROXYCHROMEN-2-ONES

The mass spectra of the hydroxychromenones, e.g. umbelliferone (III), are distinguished merely by an increase in the number of carbonyl groups ejected[1,2] (Scheme 2). As with coumarin itself, elimination of 28 amu at the second stage is accompanied by removal of 29 amu (formyl or carbonyl plus hydrogen). In contrast to the unsubstituted chromenone, later eliminations of a carbonyl group drop sharply in intensity (Table 2).

Scheme 2

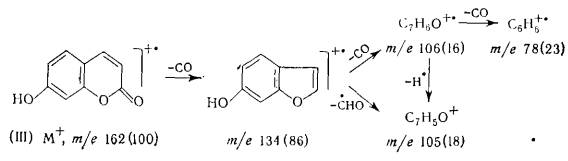


Table 2. Values of m/e and $100I/I_{max}$ for peaks due to ions involved in elimination of carbonyl groups in the mass spectra of hydroxychromen-2-ones.

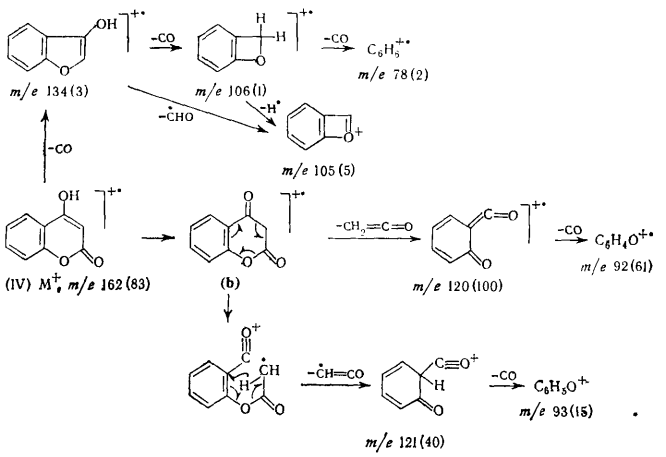
Derivative	M+	M—CO	M—2CO	M—2CO—H	M—3CO	M—4CO
4-Hydroxy (IV)	162 (86)	134 (3)	106 (1)	105 (5)	78 (3)	—
6-Hydroxy	162 (100)	134 (69)	106 (6)	105 (5)	78 (18)	—
7-Hydroxy (umbelliferone, III)	162 (100)	134 (86)	106 (16)	105 (18)	78 (20)	—
6,7-Dihydroxy (aesculetin)	178 (100)	150 (75)	122 (3)	121 (3)	94 (8)	66 (6)

The appearance potential of the 134 ion $[M - 28]^+$ for umbelliferone (10.6 eV) is closer to that of the corresponding ion for the chromenone (11.6 eV) than that of the same ion in the case of phenol (12.3 eV), which indicates elimination of the lactonic carbonyl at the first stage of decomposition[2].

The Reviewers have observed a significant difference between the breakdown of 4-hydroxychromenone (IV) and that of other hydroxychromenones. Decomposition involves mainly elimination of 42 amu from the molecular

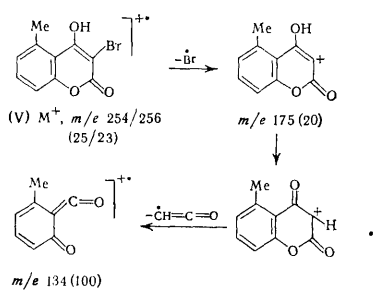
ion (the 120 peak at m/e is the most intense in the spectrum) followed by elimination of carbonyl (92 peak) (Scheme 3). Although the successive elimination of three carbonyl groups can be traced in the spectrum of the 4-hydroxy-derivative (Table 2), this process takes place to only a slight extent.

Scheme 3



On electron bombardment the molecular ion of 4-hydroxychromenone probably undergoes tautomerisation into the ion of chroman-2,4-dione (b), which then decomposes by a retrodiene reaction with elimination of a keten molecule and formation of a radical-ion having $m/e = 120$, or with removal of a keten radical and formation of an ion having $m/e = 121$. Analogous elimination of a keten molecule is evident in the mass spectrum of the monocyclic analogue of 4-hydroxychromenone—triacetic acid.

Scheme 4

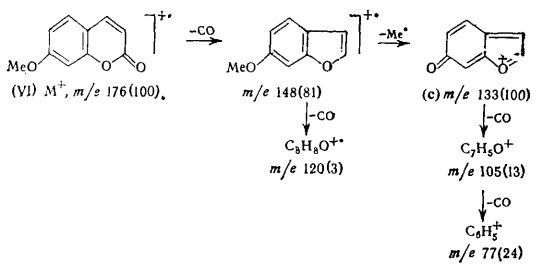


According to Johnson and Pelter[9] 3-aryl-4-hydroxychromenones also eliminate an arylketen molecule or radical on electron bombardment. With 3-bromo-4-hydroxy-5-methylchromenone (V),[10] as with the halogenated chromenones described above, the bromine atom is eliminated first, and a keten radical is subsequently eliminated after tautomeric ketonisation of the 175 ion (Scheme 4).

IV. METHOXYCHROMEN-2-ONES

The mass spectra are greatly affected by methylation of the hydroxyl in hydroxychromen-2-ones[1,2]. Although elimination of a carbonyl group is still the first stage in decomposition of the molecular ion of the methyl ether of umbelliferone—herniarin (VI)—elimination of the methyl group with formation of a 133 ion (Scheme 5, ion c), evidently stabilised by a quinonoid structure, predominates at the second stage. After this another carbonyl group is eliminated. It must be emphasised that neither methyl nor methoxyl is eliminated from the molecular ion in the case of herniarin (Table 3).[1,2,11]

Scheme 5



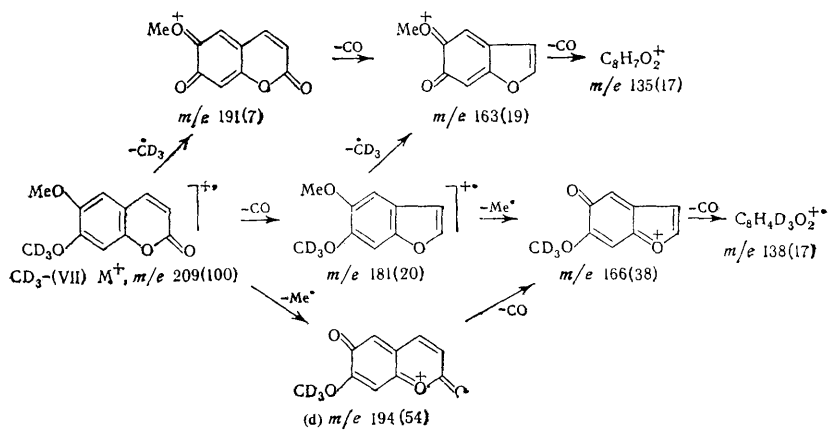
The Reviewers have observed a similar pattern in the mass spectrum of 7-hydroxy-6-methoxychromen-2-one (scopoletin), and the Australian workers[2] in that of 6,7-dimethoxychromen-2-one (scoparin) (VII). However, a significant feature of the behaviour of these compounds under electron bombardment is elimination of a methyl group from the molecular ion together with the first elimination of a carbonyl group, the peak of the $[M - CH_3]^+$ ion being more intense than that of the $[M - CO]^+$ ion. The sequence of subsequent eliminations in this mode of decomposition is included in Table 3.

Table 3. Values of m/e and $100I/I_{max}$ for peaks due to main ions in the mass spectra of methoxychromen-2-ones.

Derivative	M+	M—Me	M—CO	M—2CO	M—CO—Me M—Me—CO	M—CO—Me—CO M—Me—2CO	M—CO—Me—2CO M—Me—3CO	M—CO—Me—3CO M—Me—4CO
7-Methoxy (herniarin, VI)	176 (100)	—	148 (81)	120 (3)	133 (100)	105 (13)	77 (14)	—
7-Hydroxy-6-methoxy (scopoletin)	192 (100)	177 (43)	164 (22)	—	149 (37)	121 (14)	93 (1)	65 (4)
6,7-Dimethoxy- (scoparin, VII)	206 (100)	191 (30)	178 (20)	—	163 (30)	135 (19)	107 (20)	79 (6)

Shapiro and Djerassi[12] compared the spectra of (VII) and its 7-trideuteromethyl analogue and showed that formation of the $[M - CH_3]^+$ ion involves elimination of the methyl group predominantly from the 6-methoxyl with formation of a *p*-quinonoid 194 ion (ion (d) in Scheme 6). This observation is fully consistent with the absence of the $[M - CH_3]^+$ peak in the spectrum of herniarin and its presence in that of scopoletin. In contradistinction to this, loss of a methyl group by the $[M - CH]^+$ ion occurs with equal probability from either the 6- or the 7-methoxyl in scoparin, as is indicated by the fact that the peaks of the resulting 163 and 166 ions have approximately the same intensities as the 135 and 138 peaks in the spectrum of the 7-trideuteromethyl analogue of scoparin (Fig. 2). As with *o*-dimethoxybenzene, elimination of a formaldehyde molecule from the methoxyl is not observed here[11].

Scheme 6



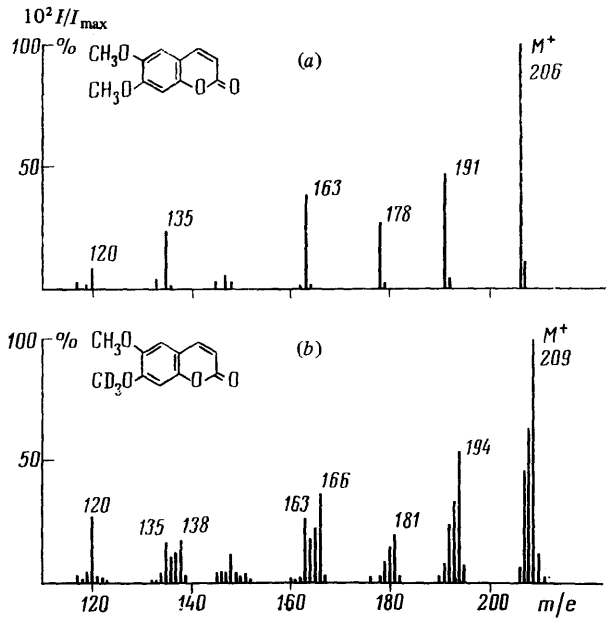


Figure 2. Mass spectra of: *a*) scoparin; *b*) 7-trideuteromethylscoparin.

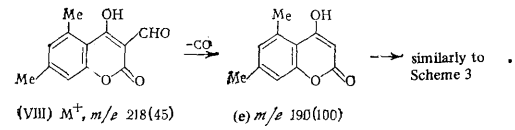
The fragmentation paths are little affected by introduction of a methyl group at any of the carbon atoms[10] or of a 4-phenyl group in the chromenone molecule or its hydroxy- or methoxy-derivatives[13-15]. Introduction of an ethyl group, however, leads to elimination of a methyl group, which is favoured by the possibility of formation of a tropylium ion[10].

V. 3-CARBONYL-CONTAINING CHROMEN-2-ONE DERIVATIVES

Aldehydes

The only aldehyde derivative whose mass spectrum has been reported—3-formyl-4-hydroxy-5,7-dimethylchromen-2-one (VIII) [10]—undergoes elimination of a carbonyl group with formation of the 190 ion (e) (Scheme 7) (whose peak is the most intense in the spectrum), having the structure 4-hydroxy-5,7-dimethylchromenone. Subsequent breakdown of the ion is analogous to that described for 4-hydroxychromenone (Scheme 3).

Scheme 7



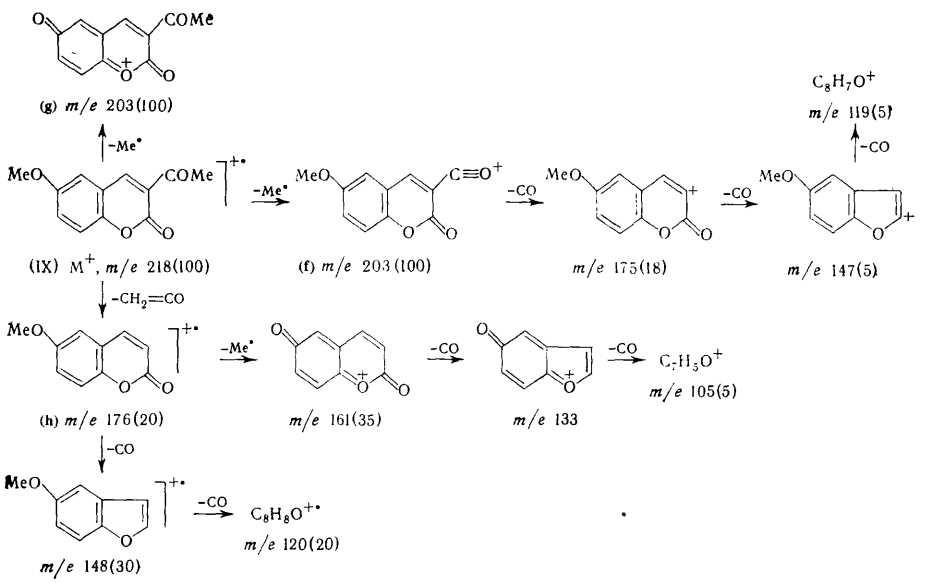
Ketones

The most intense peaks in the mass spectrum of 3-acetyl-6-methoxychromen-2-one (IX) [10] are due to the molecular ion and to the 203 ion $[M - CH_3]^+$. Formation of the latter is due to the equal probability of loss of methyl from the acetyl group (Scheme 8, ion f) and from the 6-methoxy-group (ion g). This is followed by the repeated loss of carbonyl groups. The molecular ion of the ketone (IX) can break down also by elimination of a keten molecule with formation of the 176 ion (h), which then either loses successively a methyl group and two molecules of carbon monoxide or else eliminates the two molecules (Scheme 8).

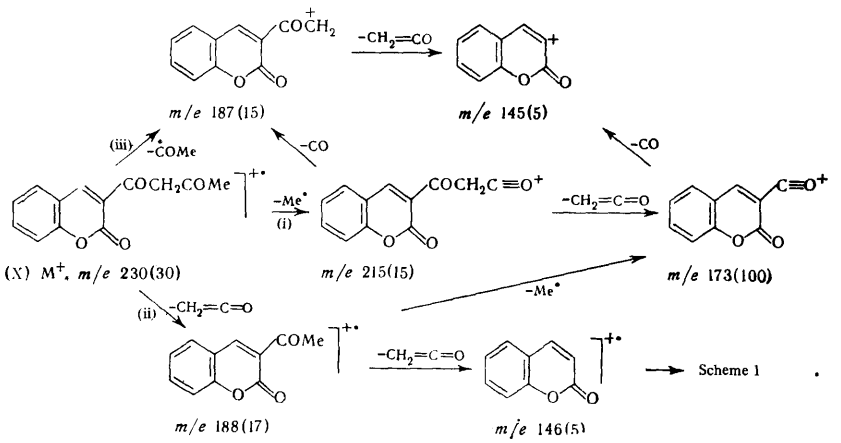
3-Acetoacetylchromen-2-one (X) can break down in three ways[10] (Scheme 9): (i) successive loss of a methyl group, a keten molecule, and a carbonyl group involves formation of a 145 ion analogous to the 175 ion formed from the ketone (IX) (Scheme 8); (ii) preliminary elimination of a keten molecule entails formation of an ion identical with the molecular ion of 3-acetylchromen-2-one, which then loses either another keten molecule or a methyl group followed by carbonyl; or (iii) preliminary elimination of an acetyl group and then a keten molecule yields an ion with $m/e = 145$.

Introduction of 4-hydroxyl and 6-methyl into the 3-acetoacetylchromenone has no significant effect on breakdown of the molecular ion under electron bombardment[10]. Only after elimination of the acetoacetyl group does decomposition characteristic of 4-hydroxychromenone begin.

Scheme 8



Scheme 9

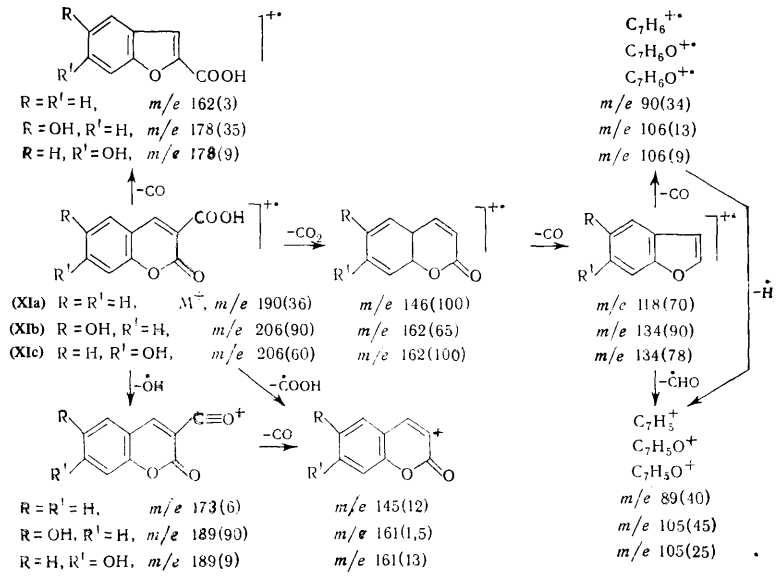


Acids and their Esters

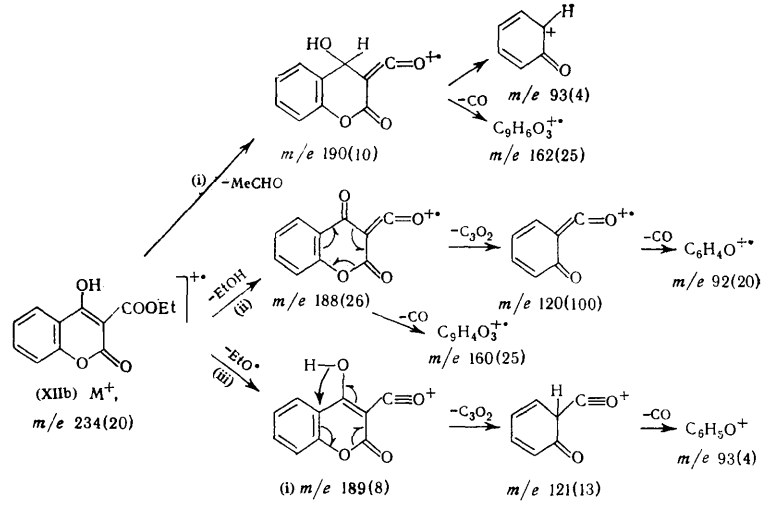
The Reviewers have found three independent modes of decomposition for 2-oxochromen-3-carboxylic acid (XIa) and its 6- and 7-hydroxy-derivatives (XIb) and (XIc) (Scheme 10). The first of these (traditional for coumarins), involving successive elimination of a carbonyl group, is strongly repressed. The second begins with elimination of a carboxyl as OH–CO and COOH (the peak due to the $[M - OH]^+$ ion is extraordinarily intense (90%) in the spectrum of the 6-hydroxy-derivative (XIb)). This is accompanied by very slight removal of formic acid to give the ion $[M - HCOOH]^+$. The third and main mode of breakdown of the oxochromencarboxylic acid entails detachment of a molecule of carbon dioxide, probably via a four-membered transition state. The $[M - CO_2]^+$ ion, which has the structure of the corresponding chromenone, breaks down further with successive elimination of carbonyl groups (elimination of a formyl group again accompanies elimination of a carbonyl group).

The pattern of fragmentation is still more complicated when the carboxyl has been esterified, as a consequence of breakdown of the alkoxycarbonyl group. Johnstone et al.[10] reported the mass spectra of methyl (XIIa) and ethyl (XIIb) 4-hydroxy-2-oxochromen-3-carboxylates, and of the 8-methyl (XIII) and 5,7-dimethyl (XIV) derivatives of (XIIa). Esters that were unsubstituted in the aromatic ring—(XIIa) and (XIIb)—could decompose in three independent ways (Scheme 11): (i) initial elimination of an aldehyde molecule is followed by cleavage of the heterocyclic ring and migration of a hydrogen atom to the charged particle or loss of a carbonyl group; (ii) initial elimination of an alcohol molecule from the alkoxycarbonyl group is followed by rupture of the heterocyclic ring (due to elimination of a carbon suboxide molecule) and then elimination of a carbonyl group or by immediate elimination of carbonyl from position 2 or 4; and (iii) initial detachment of alkoxyl gives the ion (i), which then loses a carbon suboxide molecule and a carbonyl group in succession.

Scheme 10



Scheme 11



The Reviewers suppose that the latter two routes may result from initial tautomeric ketonisation of the molecular ion followed by elimination of an alcohol molecule or alkoxyl and then a retrodiene decomposition, accompanied in (iii) by migration of a hydrogen atom to the charged particle (see Scheme 3).

Methylation of the aromatic ring in the ester (XIIa)—to give (XIII) and (XIV)—has no significant effect on the modes of decomposition of their molecular ions under electron bombardment, and is apparent merely in a decrease in intensity of peaks due to ions of type (i).

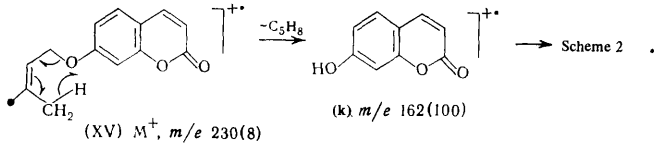
Introduction of an *O*- or a *C*-alkyl or -cycloalkyl substituent with a large number of carbon atoms into the chromenone molecule complicates appreciably the pattern of fragmentation of the molecular ion, since processes involving rupture of bonds in these substituents begin to play a significant part. Direct loss of a carbonyl group by the molecular ion becomes less characteristic, and often this process becomes apparent only in the later stages of decomposition.

VI. *O*-ALKYLATED CHROMEN-2-ONES

Naturally occurring chromenones, which usually contain an isopentenyl or a still longer isoprenoid residue attached to the ring through oxygen, are characterised by extreme ease of decomposition under electron bombardment. As a consequence, peaks in the range of high mass numbers are usually weak in their mass spectra. Thus according to Bohlmann et al.[16] 7-isopentenyloxychromen-2-one (XV) first loses the side-chain as a result of rupture of the carbon–oxygen bond with migration of a hydrogen atom to the charged particle. The 162 ion (k) thus formed

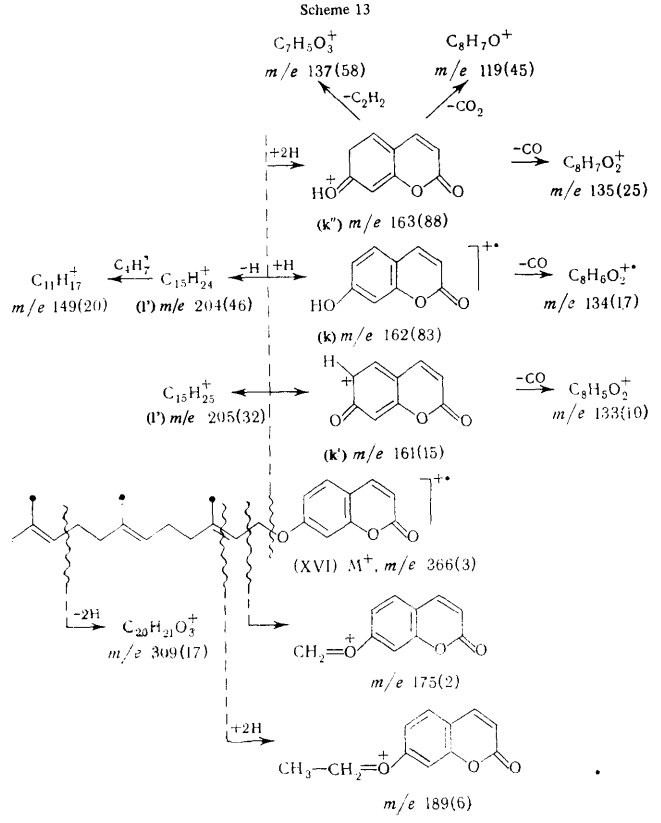
(Scheme 12) is identical with the molecular ion of umbelliferone (III), and subsequently breaks down as described above (Scheme 2 and Table 2).

Scheme 12



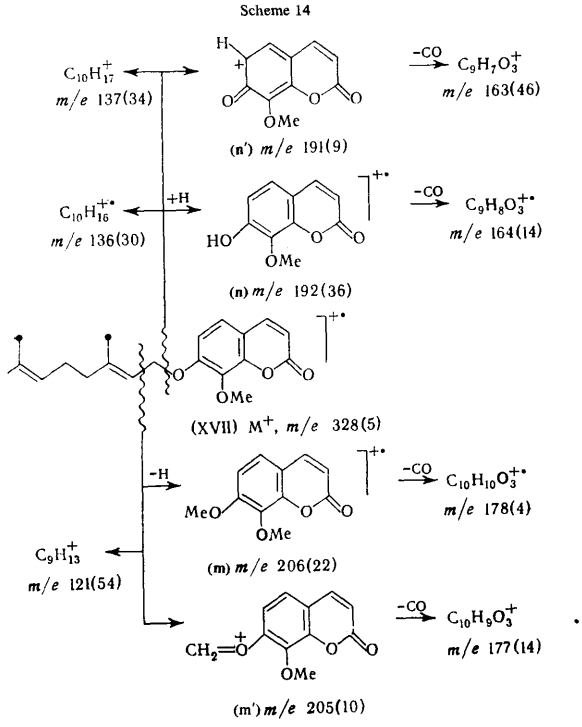
The Reviewers have found a similar situation in the mass spectrum of umbelliprenin (XVI). Cleavage of the side-chain at the carbon–oxygen bond with migration of a hydrogen atom to the charged fragment gives the 162 ion (k), accompanied by the 161 and 163 ions (k′) and (k″) formed respectively by simple rupture of the carbon–oxygen bond and by such rupture with migration of two hydrogen atoms to the charged particle. Localisation of the charge on the side-chain residue yields the 204 and 205 ions (l) and (l′) (Scheme 13).

Scheme 13

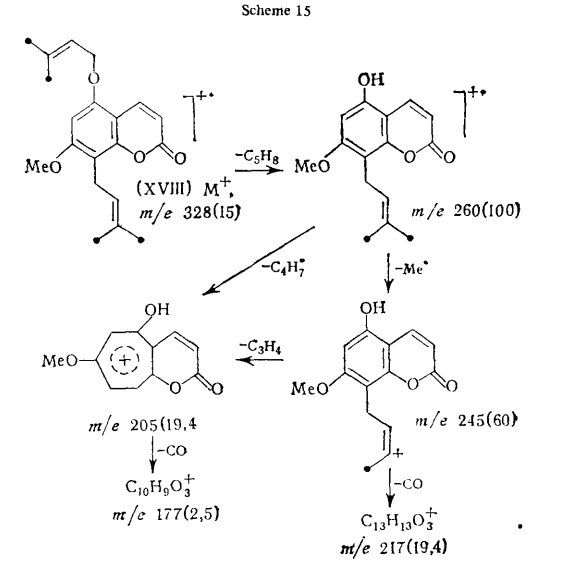


It must be borne in mind, however, that a long side-chain may break into fractions as a result of cleavage of allyl bonds. Nor can the possibility of migration of double bonds along the carbon chain be excluded. This is probably responsible for the peaks due to 309, 267, and 254 ions (17%, 2%, and 4%) in the spectrum of umbelliprenin. A 175 ion (2%) is formed by simple cleavage of the α-carbon–carbon bond, and corresponds to a deprotonated form of the molecular ion of herniarin. The ion (k) and the accompanying ions (k′) and (k″) then eliminate carbonyl groups in stages.

Scheme 14

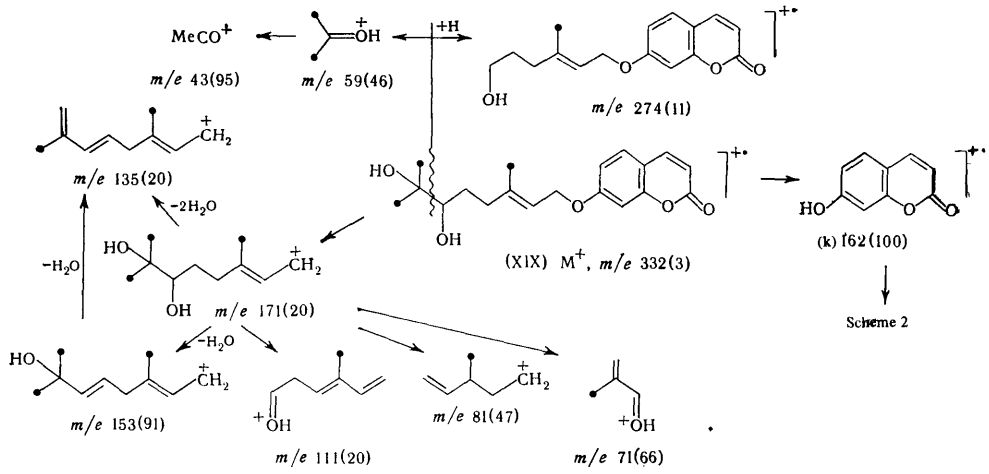


Scheme 15



In contrast to the above, according to Barnes and Occolowitz[2] collinin—7-geranyloxy-8-methoxychromen-2-one (XVII)—undergoes α-cleavage of the carbon chain with migration of a hydrogen atom to the charged fragment and formation of a 206 ion (m) identical with the molecular ion of 7,8-dimethoxychromen-2-one (Scheme 14). This ion is accompanied by a 205 ion (m′) formed by simple

Scheme 16

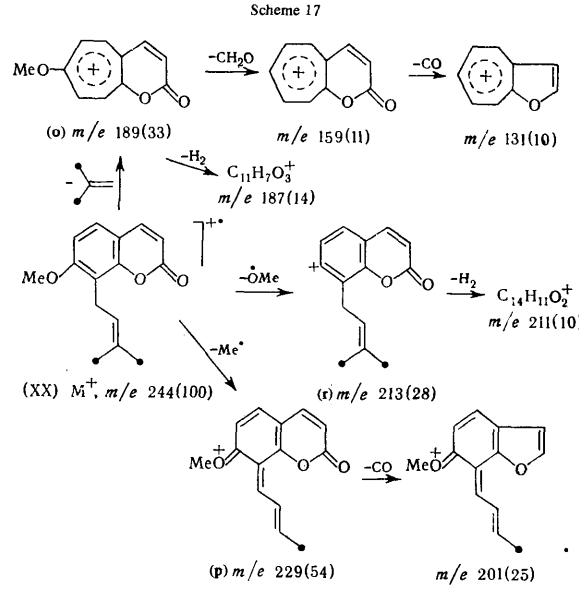


α-cleavage. With collinin the above rupture of the carbon–oxygen bond also occurs, with the formation of ions 192 and 191 (n and n'), the former identical with the molecular ion of 7-hydroxy-8-methoxychromen-2-one, and the latter with its deprotonated form. Rupture of the same bonds but with localisation of the charges on the aliphatic chain yields ions having m/e = 121, 136, and 137.

Loss of an isopentenyl substituent with migration of a hydrogen atom to oxygen has been observed also by Seshadri and Vishwapaul[17] in the mass spectrum of sesibiricin—8-isopentenyl-5-isopententyloxy-7-methoxychromen-2-one (XVIII) (Scheme 15)—isolated from *Sesili sibiricum*. Subsequent breakdown of the 260 ion is governed by the presence of the *C*-isopentenyl residue (Section VII).

Decomposition of the more complicated 7-(6,7-dihydroxy-3,7-dimethyloct-2-enyloxy)chromen-2-one (XIX) follows a similar pattern[18]. Besides rupture of the carbon–oxygen bond with migration of a hydrogen atom to the charged fragment with formation of the ion (k) (Scheme 16), the presence of an α-diol group in the side-chain stimulates formation of ions having m/e = 274, 171, 153, 135, 111, 81, 71, 59, and 53.

Scheme 17



VII. *C*-ALKYLATED CHROMEN-2-ONES

When an isopentenyl residue is directly attached to the chromenone ring system, as e.g. in osthol[1,2]—8-isopentenyl-7-methoxychromen-2-one (XX)—part of the side-chain is lost as an isobutenyl radical with formation of a tropylium ion (o) having m/e = 189 (Scheme 17), which then loses a molecule of formaldehyde from the methoxy-group (similarly to anisole[19] and methoxy-quinones[20,21]) and a carbonyl group. Successive elimination of carbonyl groups takes place only after loss of a terminal methyl from the molecular ion, i.e. from a 229 ion. Elimination of only methoxyl from the molecular ion, which has not been observed in the above cases, is evidently due to the proximity of the unsaturated isopentenyl residue. A 213 ion (r) is thus formed, which then loses a molecule of hydrogen.

Fragmentation of the isomeric suberosin—6-isopentenyl-7-methoxychromen-2-one (XXI)—is in principle very similar to that of osthol[22,23]. The difference in the position of the isopentenyl residue is reflected, however, in a fairly considerable change in intensity of several peaks, especially those due to breakdown of the side-chain (Table 4).

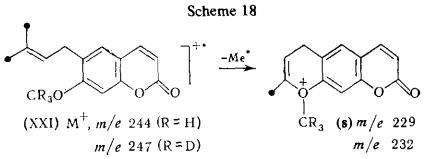
Table 4. Values of m/e and $100I/I_{max}$ for the peaks due to the main ions in the mass spectra of osthol and suberosin.

Compound	M+	M—Me	M—CH_2O	M—MeO	M—C_4H_7	M—C_5H_9
Osthol (XX)	244 (100)	229 (54)	214 (5)	213 (28)	189 (33)	176 (7)
Suberosin (XXI)	244 (97)	229 (100)	214 (3)	213 (4)	189 (13)	176 (5)

Compound	M—C_5H_9	M—Me—CO	M—C_4H_7—H_2	M—C_4H_7—CH_2O	M—C_4H_7—CH_2O—CO
Osthol (XX)	175 (8)	201 (25)	187 (14)	159 (11)	131 (10)
Suberosin (XXI)	175 (4)	201 (3)	187 (3)	159 (4)	131 (3)

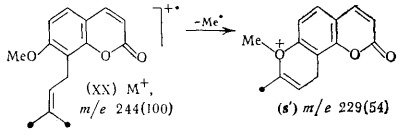
From the mass spectrum of the trideuteromethyl analogue of suberosin, in which the 229 peak of the $[M - 15]^+$ ion is almost completely (98%) displaced to 232, MacLeod confirmed experimentally[23] that methyl is eliminated from the side-chain. He assigned the cyclic structure (s) (Scheme 18) to this ion. For the rest his results are consistent with the scheme of decomposition of osthol (Scheme 17).

Scheme 18



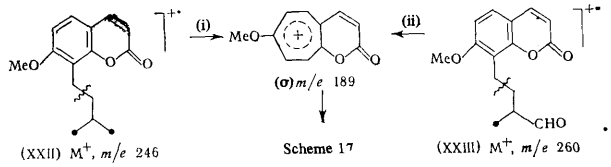
It cannot be excluded that the $[M - 15]^+$ ion from osthol also has an angular cyclic structure (s') (Scheme 19). The molecular ion of the recently reported 8-isopentenyl-5,7-dimethoxychromen-2-one decomposes similarly to osthol and suberosin on electron bombardment[24].

Scheme 19



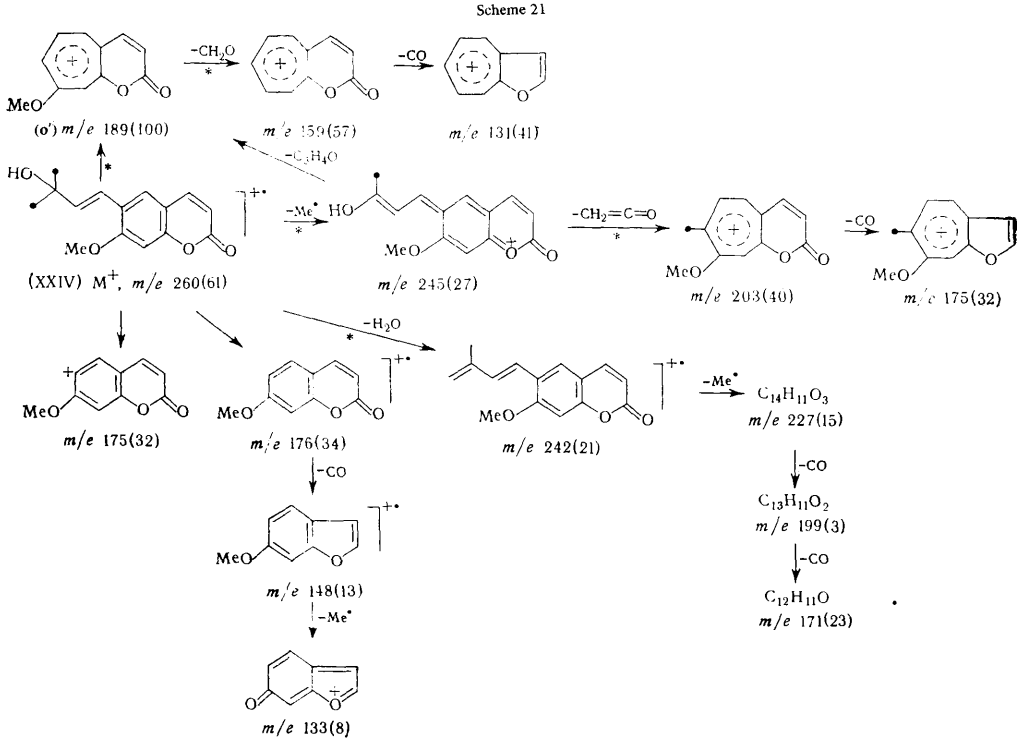
The peak due to the $[M - CH_3]^+$ ion is of negligible intensity in the spectrum of dihydro-osthol (XXII),[2] owing to the saturated character of the side-chain, and is completely absent from the spectrum of dihydrosuberosin[23], which can be attributed to the impossibility of stabilising the charge by a conjugated system of double bonds. Elimination of methoxyl as formaldehyde is also absent. The main mode of decomposition of dihydro-osthol[2] and dihydrosuberosin[23] is elimination of the side-chain by rupture of the benzylic carbon–carbon bond with formation of the tropylium ion (o) having $m/e = 189$ (Scheme 20i). Similar decomposition with formation of the ion (o) is evident also in the mass spectrum of 8-3'-formylbutyl-7-methoxychromen-2-one (XXIII)[25] (Scheme 20ii). It is curious that the $[M - CH_3]^+$ ion is not formed even in this case.

Scheme 20



Hydroxylation or epoxidation of the side-chain causes additional decomposition in the side-chain, as has been shown above for the derivative (XIX) (Scheme 16). Thus Australian workers have shown[22] that the molecular ion of suberenol—6-(3-hydroxy-3-methylbut-1-enyl)-7-methoxychromen-2-one (XXIV)—breaks down along three main paths (Scheme 21). (i) Elimination of a methyl group from the side-chain is followed by detachment of C_3H_4O and migration of a hydrogen atom to the charged fragment. The resulting tropylium ion (o') having $m/e = 189$ (whose peak is the strongest in the spectrum) can also be obtained directly from the molecular ion in a single-stage process analogous to that described above. The ion (o') loses further the methoxy-group as formaldehyde, and then a carbonyl group; the 245 ion $[M - CH_3]^+$ also loses a keten molecule, being converted into a 203 ion and subsequently eliminating a carbonyl group. (ii) Loss of the whole side-chain results from simple rupture of the carbon–oxygen bond (175 ion) or with migration of a hydrogen atom to the charged fragment

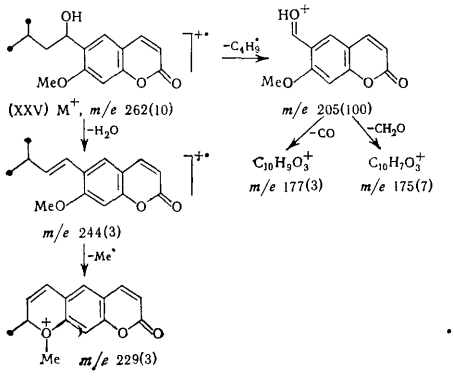
Scheme 21



through a six-membered transition state (176 ion). The 175 peak may be composite, with its second component arising from elimination of a carbonyl group from the 203 ion. The 176 ion then loses carbonyl and methyl. (iii) Loss of a water molecule by the molecular ion leads to formation of a 242 ion, from which one methyl and two carbonyl groups are then split off (the methyl probably from the side-chain). The mass spectrum of suberenol (XXIV) given by MacLeod[23] differs from the above merely in a considerably less intense peak due to the ion (o').

The mass spectrum of 6-(1-hydroxy-3-methylbutyl)-7-methoxychromen-2-one—tetrahydrogeijerin (XXV)—is very meagre[23]. The most intense peak is due to the 205 ion $[M - C_4H_9]^+$ ion (Scheme 22), which then loses a formaldehyde molecule or a carbonyl group. Another mode of decomposition of the molecular ion involves detachment of a water molecule followed by a methyl group. All the peaks due to these ions, including the molecular ion, are weak.

Scheme 22



In contrast, the mass spectrum of 6-(2,3-dihydroxy-3-methylbutyl)-7-methoxychromen-2-one—dihydrodihydroxysuberenol (XXVI) [23]—like that of the α-glycol (XIX) described earlier (Scheme 16), contains a considerable number of peaks due to ions formed by the rupture of bonds in the side-chain. The modes of decomposition indicated in Scheme 23 are supported by the mass spectra of the trideuteromethyl and 2-deuteroxyl analogues, as well as by the presence of many metastable peaks in the spectra.

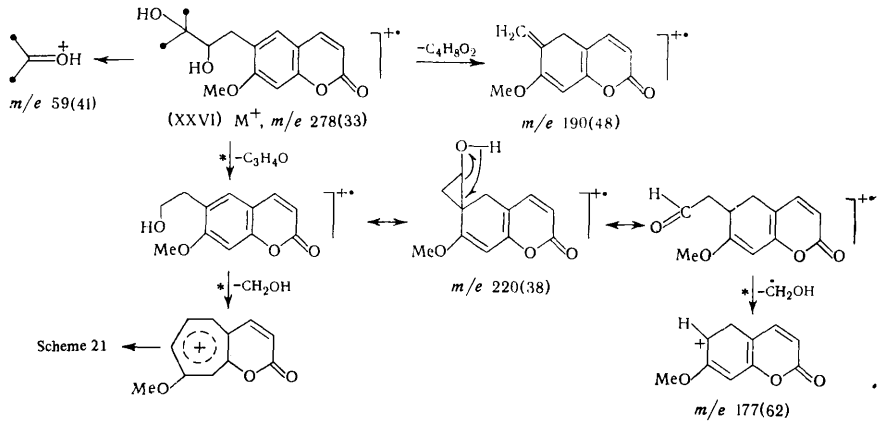
The same compound was isolated by Abyshev et al.[26] from *Prangos ulopteria* D.C. and termed *ulopterol*. Its mass spectrum corresponds essentially to Scheme 23. The spectrum of the isomeric 8-(2,3-dihydroxy-3-methylbutyl)-7-methoxychromen-2-one—merancin hydrate (XXVII)—is described in the same paper. The spectra of the isomers are very similar, differing mainly in the relative intensities of peaks due to individual ions. The chief difference is that the most intense peak in the spectrum of ulopterol is due to the 220 ion, whereas in the spectrum of merancin hydrate the 177 peak is the strongest.

According to Chakraborty et al.[27] the molecular ion of 8-(2,3-dihydroxy-3-methylbutyl)-5,7-dimethoxychromen-2-one—mexoticin (XXVIII), isolated from *Murraya exotica* L.—breaks down somewhat differently. In this case the most characteristic process is loss of the whole side-chain at position 8 with migration of a hydrogen atom to the charged fragment and formation of a 206 ion isomeric with ion (m) (Scheme 14). Rupture of the benzyl bond gives the tropylium ion (o") at 219 (Scheme 24), but simultaneous migration of a hydrogen atom to the charged fragment gives a 220 ion. The above cleavage of the α-glycolic carbon–carbon bond also occurs, with the appearance in the spectrum of peaks due to ions at 249 (t) and 59.

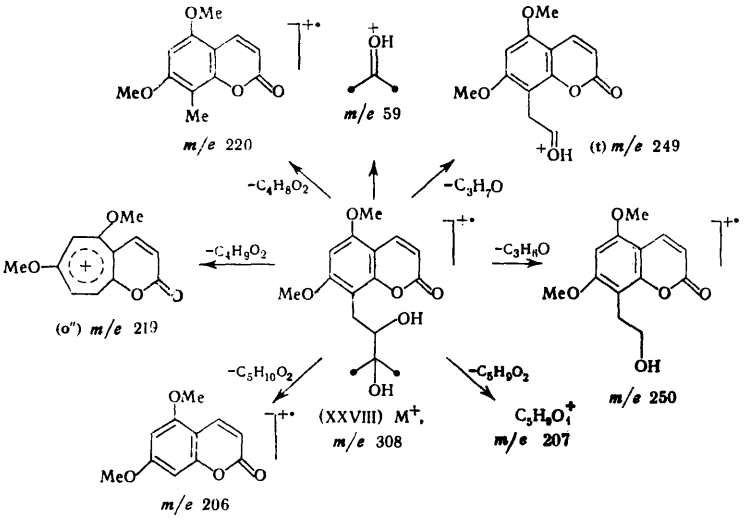
A formally similar but essentially different pattern is observed in the mass spectra of the monoacetates of ulepterol (XXIX) [26] and of merancin hydrate (XXX), [28] the latter isolated from *Prangos ferulacene* L. Decomposition can take place in two ways (Scheme 25) on electron bombardment: (i) elimination of a molecule of acetic acid from the molecular ion with formation of a 260 ion—respectively identical and isomeric with the molecular ion of suberenol—which breaks down further according to Scheme 17 or 21; or (ii) rupture of the α-glycolic carbon–carbon bond accompanied by elimination of a keten molecule, leading to the formation of ions 59 and 219. As in previous cases, the mass spectra of positional isomers (6- or 8-substituted) differ only in the relative intensities of peaks due to individual ions: for example, the most intense peak in the spectrum of (XXIX) is due to the 189 ion, but the most intense in the spectrum of (XXX) is at 219. Acetylation of the second hydroxyl in merancin hydrate has no significant effect on the decomposition of the diacetate on electron bombardment[28].

The mass spectrum of 6-(2,3-epoxy-3-methylbutyl)-7-methoxychromen-2-one—epoxysuberosin (XXXI) [23]—represents a still more complicated process, involving

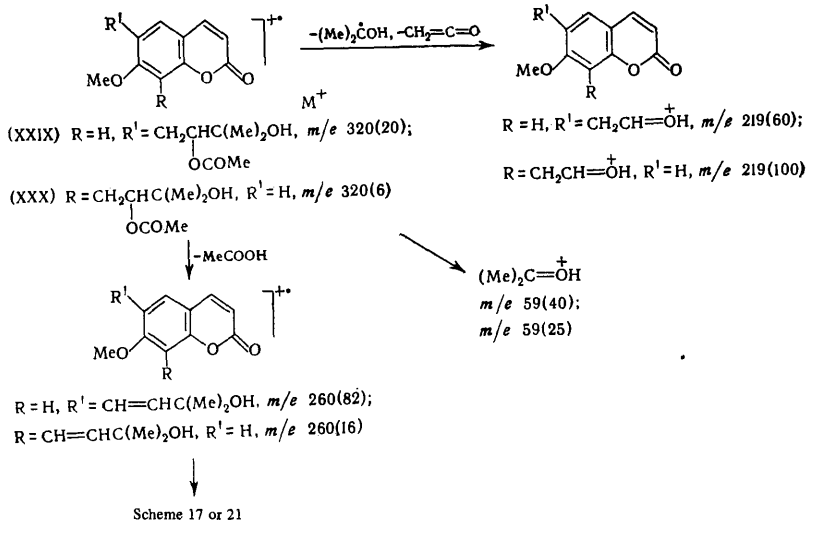
Scheme 23



Scheme 24



Scheme 25

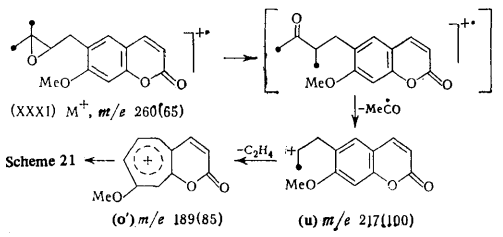


Scheme 17 or 21

a pinacolinic type of rearrangement in the side-chain of the molecular ion followed by ejection of an acetyl group and formation of the 217 ion (u) (Scheme 26). The latter ion then eliminates a molecule of ethylene and is converted into the tropylium ion (o') (189), which decomposes further in conformity with Scheme 21. This route is confirmed by the mass spectrum of the trideuteromethyl analogue and by the presence of many metastable peaks.

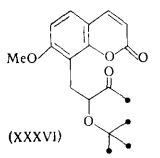
MacLeod's results[23] for the high-resolution mass spectrum of 7-methoxy-6-(3-methyl-2-oxobutyl)chromen-2-one (XXXII) (Scheme 32) and the absence of the elimination of a C_3H_7 radical (43 amu) from the molecular ion indicate that the epoxide ring does not undergo direct cleavage. They are inconsistent with Bohlmann and Rode's studies[29] of the mass spectra of 8-(2,3-epoxy-3-methylbutyl)-5,7-dimethoxychromen-2-one (XXXIII) and 8-(2,3-epoxy-3-methylbutyl)-7-isopentenyloxy-5-methoxychromen-2-one (XXXIV), both isolated from *Libanotis buchtormenis*. The latter workers regard elimination of 43 amu from the molecular ions of these two compounds as involving preliminary cleavage of the epoxide ring and formation of an ion of type (v) (at 247 and 301 respectively) (Scheme 27). Furthermore, Bohlmann and Rode[29] consider formation of the tropylium ion (o"), whose peak at 219 is the strongest in the spectrum of (XXXIII), to result from a single-stage elimination of the side-chain by cleavage of the benzylic carbon–carbon bond. Another discrepancy must be noted between the two sets of results. Bohlmann and Rode find in the spectrum of (XXXIII) quite clear evidence of the elimination from the molecular ion of an acetone molecule followed by formaldehyde (peaks at 232 and 202), whereas peaks due to the corresponding ions are almost completely absent from the spectrum of (XXXI).[23] The spectrum of (XXXIV), moreover, reveals elimination of the isopentenyl residue with migration of a hydrogen atom to the charged fragment and formation of the 7-dimethyl analogue of the molecular ion of (XXXIII), which then decomposes similarly to the latter.

Scheme 26



A rearrangement similar to that described by MacLeod for the epoxide (XXXI) has been examined by Kutney et al.[30] for 6-(1,2-epoxy-3-methylbut-3-enyl)-7-methoxychromen-2-one (XXXV), whose molecular ion eliminates a formyl radical. The $[M - CHO]^+$ ion, whose peak at 229 is the most intense in the spectrum, then loses either methyl to form a 214 ion or C_3H_4 with conversion into the ion (o') (Scheme 28). However, it is also possible that this last ion (o') is obtained as a result of fission of the epoxy-group to give a keto-form of the molecular ion, which is supported by the fairly intense peak due to the 69 ion.

Besides the above chromenones containing isoprenoid side-chains Abyshev et al.[31] described an optically inactive chromenone $C_{18}H_{22}O_5$, which they had isolated from *Prangos ferulaceae* L. and termed *pranferin*. On the basis of its chemical reactions and ultraviolet, infrared, and nuclear magnetic resonance spectra they regarded this compound (XXXVI) as 8-(2-t-butoxy-3-oxobutyl)-7-methoxychromen-2-one

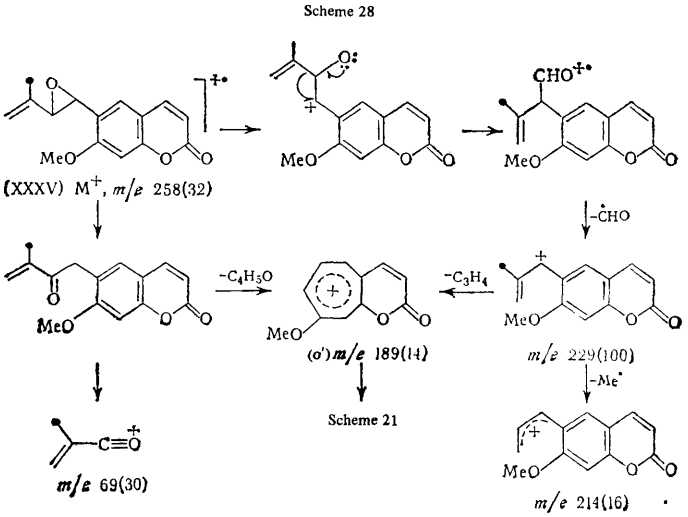


The authors state that this structure agrees well with the mass spectrum, which they do not analyse in detail. However, the one- and two-stage elimination of acetic acid from the $[M - 15]^+$ ion, clearly traceable in the spectrum, completely contradicts the proposed structure for the side-chain at position 8, although the presence of a fairly intense peak due to a 189 ion confirms that pranferin is a 7-methoxychromen-2-one derivative. Furthermore, the proposed[31] formula (XXXVI) contains an asymmetric carbon atom, which is inconsistent with the stated absence of optical activity, whereas other chromenones isolated by these workers from the same plant and containing an analogous

$$-CH_2-\underset{|}{CH}-O-$$

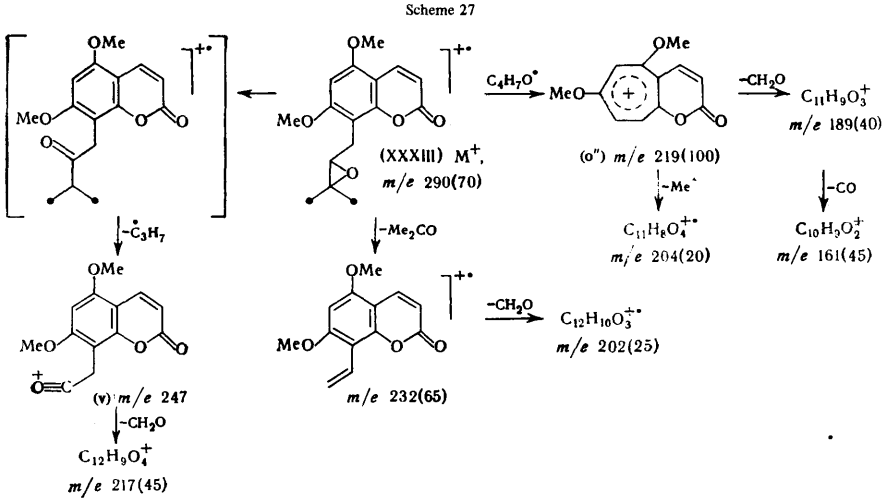
group are optically active[28].

Scheme 28

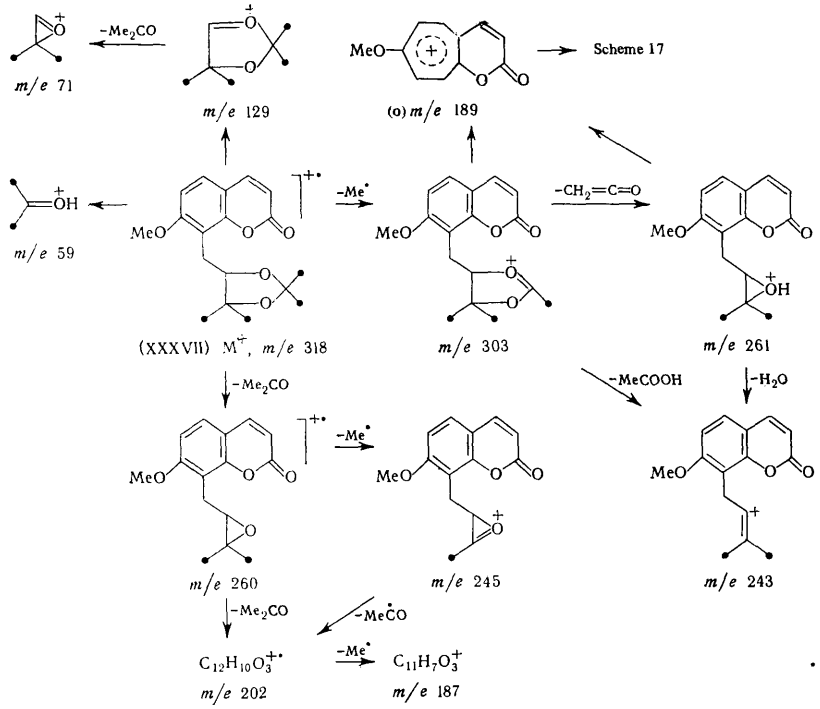


Nikonov and Saidzhadzhiev[32] analysed the n.m.r. data given by Abyshev et al.[31], and concluded that pranferin is an acetonide of merancin hydrate (XXXVII), which was confirmed by synthesis from osthol via the corresponding epoxide and merancin hydrate. The published mass spectrum of pranferin[31] agrees well with formula (XXXVII) (Scheme 29).

Scheme 27

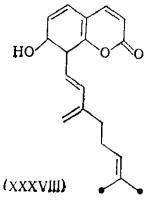


Scheme 29



VIII. CHROMEN-2-ONES CONTAINING CYCLOALKYL SUBSTITUENTS

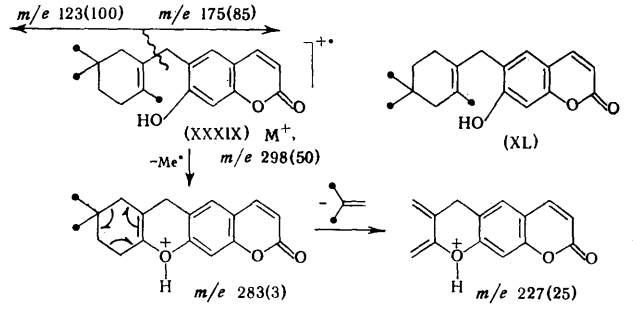
The first representative of this type of chromenone whose mass spectrum has been reported is peucenol (peumorisine), isolated from the roots of *Peucedanum morisonii* Bes. The Reviewers originally assigned to it the structure 8-(7-methyl-3-methylenocta-1,6-dienyl)-7-hydroxychromen-2-one[33]



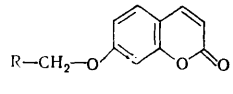
(XXXVIII) ,

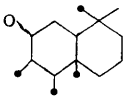
but this formula was not confirmed by subsequent study of the n.m.r. spectrum. Examination of the n.m.r. and mass spectra of peucenol suggested a cyclic structure, either (XXXIX) or (XL) [34] (Scheme 30), both consistent with biogenetic considerations. Perel'son later showed unambiguously, on the basis of the nuclear magnetic double resonance spectrum, that peucenol has the structure (XXXIX), in good agreement with the mass spectrum: detachment of the carbocyclic substituent by rupture of the benzylic bond yields 175 and 176 ions of tropylium type (by simple rupture and by rupture with migration of a hydrogen atom to the charged fragment). If the charge resulting from this process is localised on the other part of the molecule, a 123 ion is formed. The peaks at 283 and 227 are due to loss by the molecular ion of a methyl group (probably that adjacent to the double bond of the cyclohexene ring) followed by retrodiene decomposition in the cyclohexene ring with ejection of isobutene.

Scheme 30

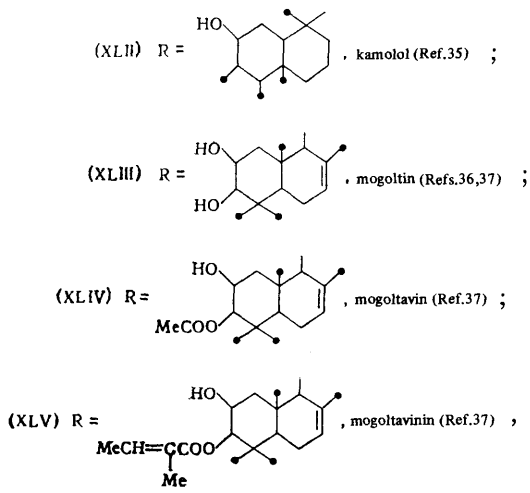


During recent years mass spectra have been reported for the umbelliferone derivatives (XLI)-(XLV) isolated from *Ferula peninervis*[35] and *Peucedanum mogeltovicum* Korov[36,37], in which the phenolic hydroxyl has been alkylated with sesquiterpenoid bicyclic residues. The mass spectra of all these compounds



(XLI)† R =  , kamolone (Ref.35) ,

† From biogenetic considerations Paknikar and Kirtany[59] have recently assigned to the sesquiterpenoid substituent of kamolone the structure decahydro-1,2,4a,5-tetramethyl-6-oxonaphthylmethylene.

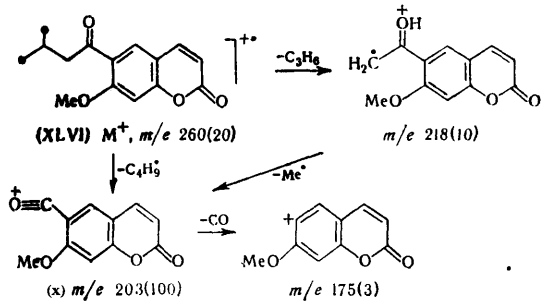


indicate rupture of a carbon–oxygen bond and the α-carbon–carbon bond in the side-chain, both alone and accompanied by migration of hydrogen atoms. The charge is localised on either moiety, chromenone or sesquiterpenoid. The spectra, of course, contain many peaks due to ions formed by further breakdown of the sesquiterpenoid ions, but information on the structure of this part of the molecules is obtained mainly from an analysis of the n.m.r. spectra.

IX. CHROMEN-2-ONES CONTAINING A KETO-GROUP IN THE SIDE-CHAIN

Study by MacLeod[23] of the mass spectra of two isomeric ketones—7-methoxy-6-(3-methyl-1-oxobutyl)chromen-2-one geijerin (XLVI) and 7-methoxy-6-(3-methyl-2-oxobutyl)chromen-2-one (isogeijerin) (XXXII)—and their deuterated analogues showed that the route of decomposition of the molecular ions is significantly influenced by the position of the keto-group in the side-chain.

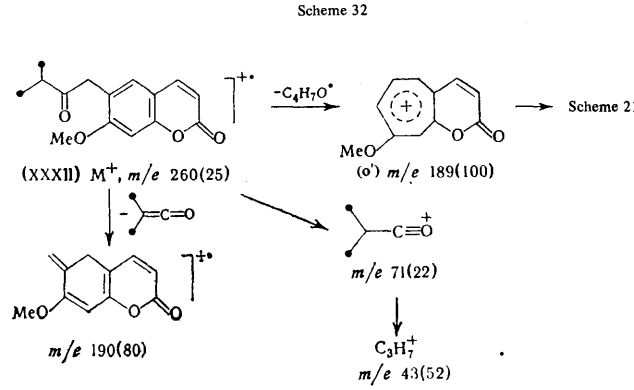
Scheme 31



The most intense peak in the mass spectrum of geijerin is due to the 203 ion (**x**), which may be formed in a single stage by elimination of an isobutyl radical or in two stages by the successive elimination of a propene molecule and a methyl group (Scheme 31).

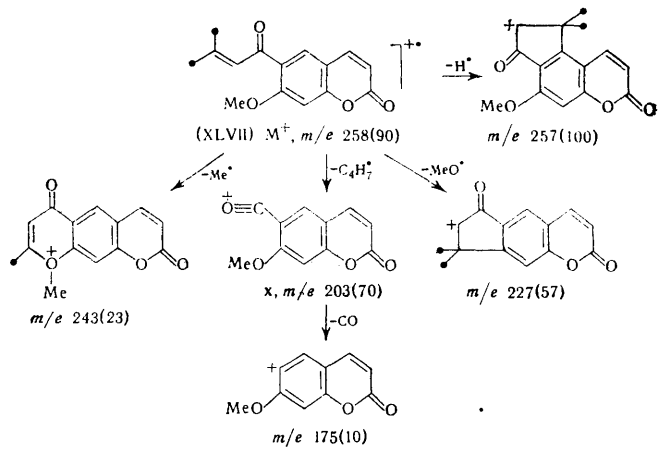
In the mass spectrum of isogeijerin, however, the strongest peak is due to the tropylium ion (**o'**) at 189, and is accompanied by a very intense peak due to a 190 ion (Scheme 32).

Scheme 32



The spectrum of 7-methoxy-6-(3-methyl-1-oxobut-2-enyl)chromen-2-one—dehydrogeijerin (XLVII)—is considerably more complicated[23] than those of the above saturated ketones. The peak due to the molecular ion is very strong, while the most intense peak is due to the ion $[M - 1]^+$, to which a tricyclic structure was assigned (Scheme 33). The molecular ion readily loses a methyl group to give a 243 ion, a methoxy-group to form a 227 ion (owing to the presence of an unsaturated substituent in the *ortho*-position), and a C_4H_7 radical to form the 203 ion (**x**).

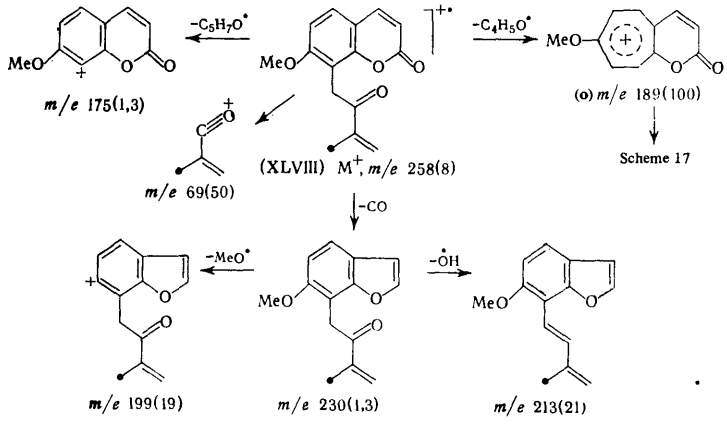
Scheme 33



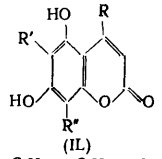
Another chromenone containing a keto-group in an unsaturated side-chain—7-methoxy-8-(3-methyl-2-oxobut-3-enyl)chromen-2-one (XLVIII), isolated from *Murraya exotica* L.—has been described by Subba Rao et al.[38] Its decomposition on electron bombardment (Scheme 34) differs significantly from that described above (Scheme 31) for the ketone (XLVI). Formation of the 189 ion (**o**) and a 69 ion, the latter produced by localisation of the charge on the side-chain residue, is accompanied by elimination from the molecular ion of a carbonyl group (230 ion) followed by elimination of methoxyl (199 ion) or of a hydroxyl resulting from enolisation (213 ion).

This type of compound includes a large group of 4-alkyl and 4-phenyl-5,7-dihydroxychromen-2-ones containing isopentenyl and various *C*-acyl radicals in the aromatic

Scheme 34



ring, isolated from *Mammea americana* L.[13,39] and from *M. africana*,[14,40] which can be represented by the general formula



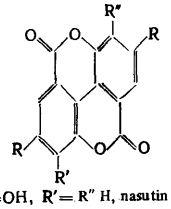
(IL)

R=H, *n*-C_3H_7, *n*-C_4H_9, s-C_4H_9, *n*-C_5H_{11} or C_6H_5.
R′=H, $Me_2C{=}CHCH_2$, iso-C_5H_7CO, iso-C_4H_9CO or s-C_4H_9CO.
R″=H, $Me_2C{=}CHCH_2$, *n*-C_5H_7CO, iso-C_4H_9CO or s-C_4H_9CO.

The decomposition of these compounds conforms in principle to the above rules, but interpretation of the mass spectra is greatly complicated by the presence of many diverse substituents, each of which makes its own contribution.

X. BICHROMENONES

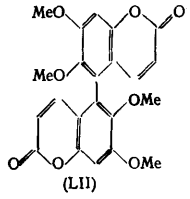
The mass spectra of the dimethyl ether (L) of nasutin A—a metabolite of termites—and the 3,3′,4-trimethyl ether (LI) of ellagic acid[41]



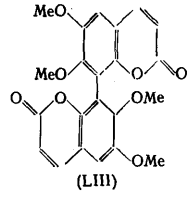
R=OH, R′= R″ H, nasutin A;
(L), R=OMe, R′=R″=H;
R=R′=R″=OH, ellagic acid;
(LI), R=R′=OMe, R″=OH,

are characterised by maximum intensities of the peaks due to the molecular ions (in the case of (L) the $[M-14]^+$ ion is present) and the detachment of methyl and methoxyl groups. Elimination of a carbonyl group is not observed.

The mass spectrum of euphorbetin—the tetramethyl ether of 6,6′,7,7′-tetrahydroxy-5,5′- or -8,8′-bichromenyl-2,2′-dione (LII) or (LIII)



(LII)



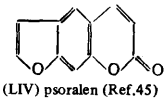
(LIII)

isolated from *Euphorbia lathyris* L.[42], is also characterised by preliminary elimination of methyl and methoxyl groups from the molecular ion. Elimination of a carbonyl group is observed only in the later stages of breakdown, and rupture of the bond between the chromen ring systems does not take place.

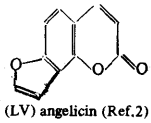
XI. FUROCHROMEN-2-ONES

The above regularities in the decomposition of chromenones under electron bombardment are largely applicable also to the more complicated furo- and pyranochromenones. The account of these will therefore be less detailed.

Unsubstituted furochromen-2-ones—the linear psoralen (LIV)[3] and the angular angelicin (LV)[2]



(LIV) psoralen (Ref.45)

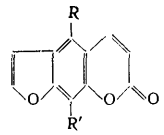


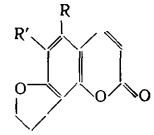
(LV) angelicin (Ref.2)

lose three carbonyl groups in succession. It is difficult to make a quantitative assessment of the results obtained by various workers with different apparatus under different experimental conditions, but a striking difference is evident in the intensities of certain peaks in the spectra of these compounds (Table 5).

The presence in the furochromenone molecule of one methoxy-group--bergapten (LVI),[2,43] xanthotoxin (LVII),[2]

isobergapten (LVIII) [44]—or of two methoxy-groups—isopimpinellin (LIX) [2,43,44] and pimpinellin (LX) [43,44]





(LVI) R = OMe, R′ = H, bergapten (Refs.2,43)
(LVII), R = H, R′ = OMe, xanthotoxin (Ref.2),
(LIX), R = R′ = OMe, isopimpinellin (Refs.2,43,44).

(LVIII), R = OMe, R′ = H, isobergapten (Ref.44),
(LX), R = R′ = OMe, pimpinellin (Ref.44),

leads to competitive elimination of a methyl group in the early stages, and this dominates the mass spectra of the latter pair of compounds. The spectra of isomers differ in the relative intensities of characteristic peaks (Tables 6 and 7).

Table 5. Values of m/e and $100I/I_{max}$ for peaks due to the main ions in the mass spectra of psoralen and angelicin.

Compound	M+	M—CO	M—2CO	M—3CO
Psoralen (LIV) (Ref.43)	186 (100)	158 (84)	130 (22)	102 (24)
Angelicin (LV) (Ref.2)	186 (72)	158 (100)	130 (24)	102 (40)

Table 6. Values of m/e and $100I/I_{max}$ for peaks due to the main ions in the mass spectra of bergapten, xanthotoxin, and isobergapten.

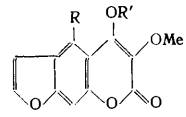
Compound	M+	M—Me	M—CO	M—Me—CO	M—2CO	M—Me—2CO	M—3CO	M—Me—3CO
Bergapten (LVI)	216	201	188	173	160	145	132	117
(Ref.2)	(100)	(38)	(21)	(78)	(4)	(40)	(3)	(3)
Xanthotoxin (LVII)	216	201	188	173	160	145	132	117
(Ref.2)	(100)	(21)	(12)	(56)	(1)	(12)	(3)	(2)
Isobergapten	216	201	188	173	—	145 (19)	—	—
(LVIII) (Ref.44)	(100)	(22)	(28)	(55)				

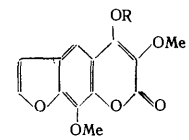
Table 7. Values of m/e and $100I/I_{max}$ for peaks due to the main ions in the mass spectra of pimpinellin and isopimpinellin.

Compound	M+	M—Me	M—2Me	M—Me—CO	M—Me—2CO
Pimpinellin (LX) (Ref.44)	246 (100)	231 (86)	216 (5)	203 (10)	175 (14)
Isopimpinellin (LIX)	246 (91)	231 (100)	216 (4)	203 (15)	175 (14)

Compound	M—Me—3CO	M—2Me—CO	M—2Me—2CO	M—2Me—3CO
Pimpinellin (LX) (Ref.44)	147 (22)	188 (10)	160 (15)	132 (6)
Isopimpinellin (LIX)	147 (9)	188 (16)	160 (16)	132 (6)

Analogous decomposition is undergone by the molecular ions of furochromen-2-ones from *Halfordia kendack* and *H. skleroxyla*, [45] containing substituents at other positions in the chromenone ring system—halkendin (LXI), norhalkendin (LXII), halfordin (LXIII), norhalfordin (LXIV), halfordinin (LXV), isohalfordin (LXVI), and norisohalfordin (LXVII)

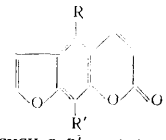


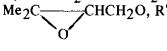
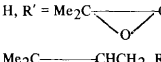
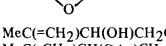


(LXI), R = H, R′ = Me, halkendin;
(LXII), R = R′ = H, norhalkendin;
(LXIII), R = OMe, R′ = Me, halfordin;
(LXIV), R = OMe, R′ = H, norhalfordin;
(LXV), R = OMe, R′ = $OCMe_2CH=CH_2$, halfordinin (Ref.45).

(LXVI), R = Me, isohalfordin;
(LXVII), R = H, norisohalfordin (Ref.45);

When the aromatic ring of the furochromenone contains more complicated substituents—isopentenyl groups (isoimperatorin (LXVIII), [43,46] imperatorin (LXIX) [43]), their epoxides (oxypeucedanin (LXX), prangenin (LXXI), [43] the epoxide of the methyl ether of alloimperatorin (LXXII) [30]), and others (gosferol (LXXIII), isolated from *Prangos ferrulaceae* Lindl, and its acetate (LXXIV), [47] the ethyl ether of oxypeucedanin hydrate (LXXV), [48] and also a furochromenone containing a formyl group in a long isoprenoid chain (LXXVI) isolated from grapefruit[25])



(LXVIII), R = $Me_2C=CHCH_2O$, R′ = H, isoimperatorin (Refs.43,46);
(LXIX), R = H, R′ = $Me_2C=CHCH_2O$, imperatorin (Ref.43);
(LXX), R =  , R′ = H, oxypeucedanin (Ref.43);
(LXXI), R = H, R′ =  , prangenin (Ref.43);
(LXXII), R =  , R′ = OMe, methyl ether of epoxyalloimperatorin (Ref.30);
(LXXIII), R = $MeC(=CH_2)CH(OH)CH_2O$, R′ = H, gosferol (Ref.47);
(LXXIV), R = $MeC(:CH_2)CH(OAc)CH_2O$, R′ = H, gosferol acetate;
(LXXV), R = $Me_2C(OEt)CH(OH)CH_2O$, R′ = H, ethyl ether (Ref.48) of oxypeucedanin hydrate;
(LXXVI), R = $Me_2(CHO)CH_2CH_2C(Me)=CHCH_2O$, R′ = H (Ref.25).

the mass spectra exhibit peaks due to ions formed in the types of decompositions considered above for the corresponding substituted chromenones.

Table 8. Values of m/e, (intensities, % on total ion current), and ratios of intensities of peaks due to characteristic ions in the mass spectra of certain furochromenone derivatives[43].

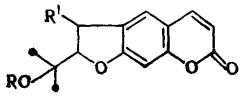
Compound	M+	M—68 *	M—84 *	M—71**	$\frac{I(M)}{I(M-68)}$	$\frac{I(M)}{I(M-84)}$	$\frac{I(M)}{I(M-71)}$
Isoimperatorin (LXVIII)	270 (0.2)	202 (5.8)	—	—	0.03	—	—
Imperatorin (LXIX)	270 (0.25)	202 (18.5)	—	—	0.01	—	—
Oxypeucedanin (LXX)	286 (5.7)	—	202 (11.6)	215 (0.6)	—	0.49	9.50
Prangenin (LXXI)	286 (5.8)	—	202 (23.2)	215 (4.3)	—	0.25	1.35

* Detachment of the side-chain and a hydrogen atom.
** Detachment of part of the side-chain.

A difference in the position of a substituent (5 or 9) is apparent only in a change in the relative intensities of the peaks due to certain ions, as can be seen from the isomers (LXVIII)–(LXXI) (Table 8). The ratio of the intensity of the peak due to the molecular ion to that of the peaks due to ionic fragments is evidently larger with the

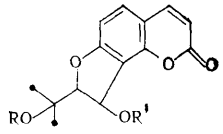
5-substituted derivatives, which will probably be useful for diagnostic purposes.

Mass spectra have been reported for mono- and di-hydroxylated linear and angular dihydrofurochromen-2-ones—marmesin (LXXVII) and its acetate (LXXVIII), angelate (deltoin) (LXXIX), senecionate (prantschimgin) (LXXX), and ω-methylthiocrotonate (seseliflorin) (LXXXI),[49] smyrniorin (LXXXII)[50,51] and its methanolysis product (LXXXIIa),[51] smyrnioridin (LXXXIII)[50,51]



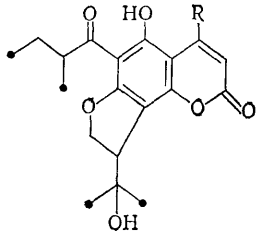
(LXXVII) R = R′ = H, marmesin;
(LXXVIII) R = MeCO, R′ = H, marmesin acetate;
(LXXIX) R = MeCH = CH(Me)CO-*trans*, R′ = H, deltoin;
(LXXX) R = Me_2C = CHCO, R′ = H, prantschimgin;
(LXXXI) R = MeSCH = CHCO, R′ = H, seseliflorin (Ref.49);
(LXXXII) R = MeCO, R′ = MeCOO, smyrniorin (Refs.50,51);
(LXXXIIa) R = MeCO, R′ = MeO, methanolysis product of smyrniorin (Ref.51);
(LXXXIII) R = MeCO, R′ = MeCH = CH(Me)COO-*trans*, smyrnioridin (Refs.50,51);

peucenidin (LXXXIV),[50] athamantin (LXXXV), and libanotin (LXXXVI)[51]



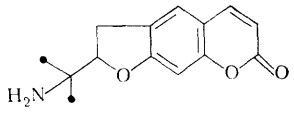
(LXXXIV) R = Me_2C = CHCO, R′ = Me, peucenidin (Ref.50);
(LXXXV) R = R′ = Me_2CHCH_2CO, athamantin (Ref.51);
(LXXXVI) R = MeCO, R′ = MeCH = C(Me)CO-*trans*, libanotin (Ref.51).

Analogous angular furochromenones



(LXXXVII) R = Ph[40];
(LXXXVIII) R = Pr[40]

isolated from *Mammea africana* G. Don are biogenetically related to the polysubstituted chromenones described in Section IX and encountered in the same plants. A mass spectrum has been reported also for the alkaloid prangosine



(LXXXIX) prangosine (Ref.52).

isolated from *Prangos pabularia* Lindl, which is a derivative of psoralen, containing a 1-amino-1-methylethyl group in the furan ring.

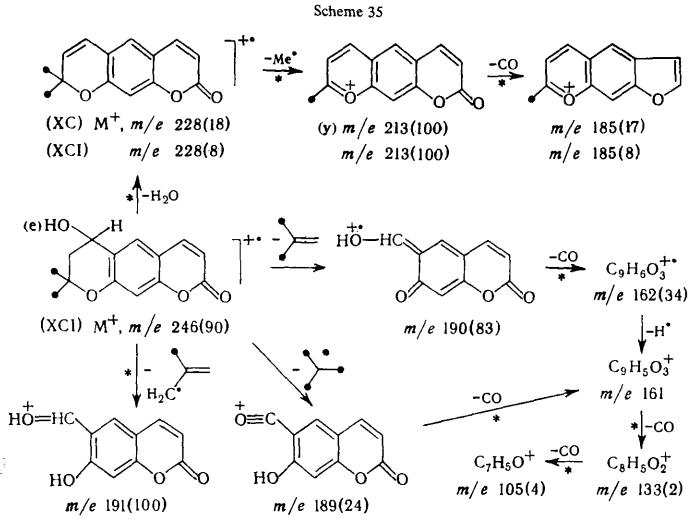
Compounds (LXXVII)–(LXXVI) undergo elimination of an acyl radical and an acid molecule (an acetyl residue is often removed as keten), and a methyl group is eliminated in the later stages of decomposition. Compound (LXXXVII) eliminates (i) a carbonyl group, an isopropoxy-group, a C_4H_9 radical from the 6-acyl substituent, and then a water molecule or (ii) an isopropoxy-group with part of the dihydrofuran ring. Only the latter type of decomposition occurs with (LXXXVIII).

Prangosine on electron bombardment eliminates a methyl group or an ammonia molecule, being converted in the latter case into an isopropenylfurochromen-2-one ion, which then loses successively a carbonyl group, a methyl group, and two more carbonyl groups.

XII. PYRANOCHROMEN-2-ONES

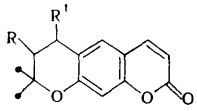
The mass spectrum of the simplest linear pyranochromen-2-one—xanthyletin (XC)[53]—indicates elimination of a methyl group to form the completely aromatised 213 ion (y) (Scheme 35), which then loses a carbonyl group.

Scheme 35



The pattern of decomposition of the molecular ion is considerably complicated when a 6-hydroxyl is introduced into dihydroxanthyletin to give (XCI).[53] Dehydration yielding an ion identical with the molecular ion of (XC) is accompanied by a retrodiene decomposition yielding a 190 ion together with migration of a hydrogen atom to or from the charged fragment (191 or 189 ion). These latter ions then eliminate a carbonyl group (Scheme 35). The corresponding ketone (XCII) decomposes similarly (Scheme 36).[53]

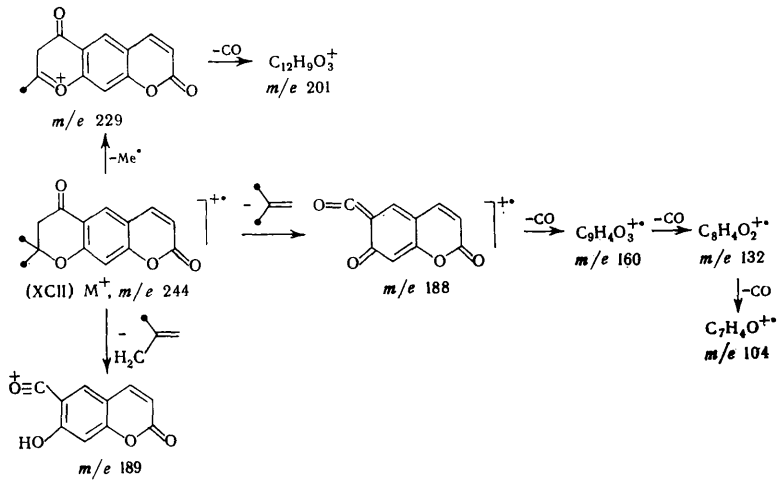
Mass spectra have been described also for the isomeric (with XCI) alcohol—agasyllol (XCIII)—its acetate (XCIV) and angelate—agasyllin (XCV)[54]—and the diacyldihydropyranochromen-2-one—andelin (XCVI)[55]



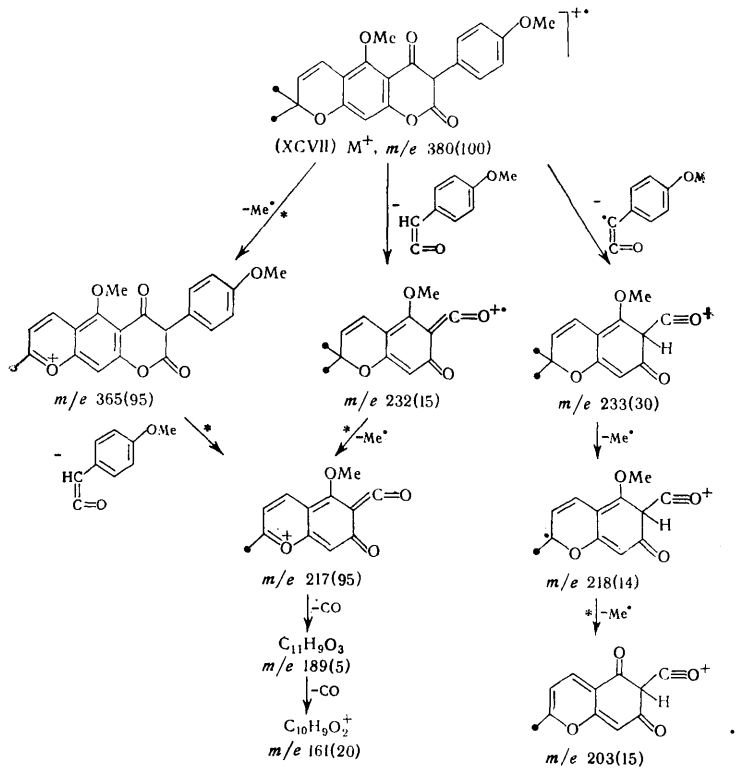
(XCIII) R = R′ = H, agasyllol;
(XCIV) R = MeCO, R′ = H, agasyllol acetate;
(XCV) R = MeCH = CH(Me)CO-*trans*, R′ = H, agasyllin (Ref.54);
(XCVI) R = Me_2C = CHCO, R′ = MeCH = C(Me)CO-*trans*, andelin (Ref.55).

Decomposition of the molecular ion of agasyllol is analogous to that described for (XCI), but breakdown of its acyl derivatives resembles that of acyl derivatives of furochromenones: i.e. the acid molecule or radical is split off. Elimination of a methyl group plays an important

Scheme 36



Scheme 37



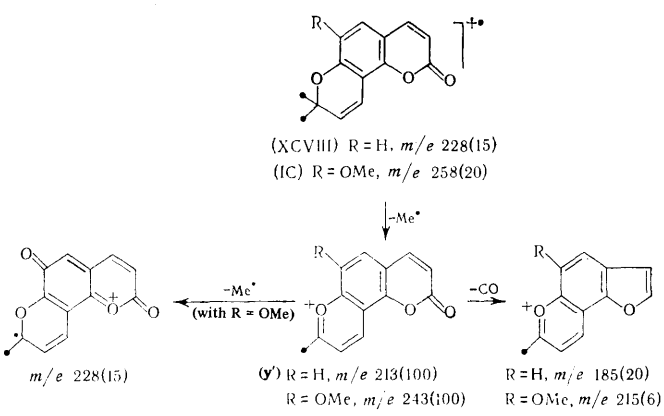
part, since, in combination with the detachment of an acid molecule, it leads to aromatisation of the pyran ring.

A more complicated example of a linear pyranochromenone is robustic acid, isolated from *Derris robusta*, which contains a 3-phenyl group (XCVII).[9,56] The breakdown of its molecular ion on electron bombardment is indicated in Scheme 37.

Angular pyranochromenones are considerably more widely distributed in Nature, so that mass spectra has been reported for an appreciably larger number of these compounds. The mass spectrum of the simplest angular pyranochromenone—seselin (XCVIII) [2]—is analogous to that of xanthyletin (XC). Elimination of a methyl group from the molecular ion yields the completely aromatised 213 ion (y'), which then loses a carbonyl group (Scheme 38). The spectrum of 6-methoxyseselin—brayelin (IC) [2]—differs from that of (XCVIII) only in the elimination of another methyl group in the second stage of decomposition, with formation of a quinonoid 228 ion (Scheme 38).

Mass spectra have been reported for dihydroseselin (C), a hydroxy-derivative (xanthogallol) (CI), and its acetate (CII), angelate (xanthogalin) (CIII),[54] senecionate[29]

Scheme 38



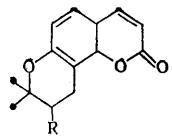
(XCVIII) R = H, *m/e* 228(15)
(IC) R = OMe, *m/e* 258(20)

m/e 228(15)

(γ') R = H, *m/e* 213(100)
R = OMe, *m/e* 243(100)

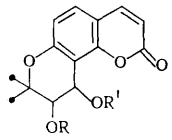
R = H, *m/e* 185(20)
R = OMe, *m/e* 215(6)

(buchtarmin) (CIV),[54] and isovalerate (CV),[29] as well as lomatin angelate (selenidin) (CVI)[57]



(C) R = H, dihydroseselin;
(CI) R = OH, xanthogallol;
(CII) R = MeCOO, xanthogallol acetate;
(CIII) R = MeCH = C(Me)COO-*trans*, xanthogalin (Ref.54);
(CIV) R = Me_2C = CHCOO, buchtarmin (Refs.29,54);
(CV) R = Me_2CHCH_2COO, xanthogallol isovalerate (Ref.29);
(CVI) R = MeCH = C(Me)COO-*trans*, selenidin (Ref.57).

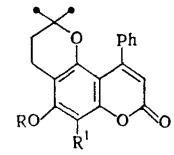
The dihydroxy-derivatives of (C) include the diol itself (kellactone) (CVII) and its diacetate (CVIII),[55] methylkellactone (CIX),[16,55] pterixin (CX),[16,55,58] its methanolysis product (CXI),[58] epoxypterixin (CXII),[58] and dihydropterixin (CXIII),[55] visnadin (CXIV), dihydrosamidin (CXV), anomalin (CXVI),[55] its monoepoxide (CXVII), and its diepoxide (CXVIII),[58] floroselin (CXIX), and its methanolysis product (CXX)[55]



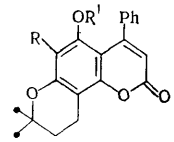
(CVII) R = R' = H, kellactone;
(CVIII) R = R' = MeCO, kellactone diacetate (Ref.55);
(CIX) R = H, R' = Me, methylkellactone (Refs.16,55);
(CX) R = MeCO, R' = MeCH = C(Me)CO-*trans*, pterixin (Refs.16,55,58);
(CXI) R = Me, R' = MeCH = C(Me)CO-*trans*, methanolysis product of pterixin;
(CXII) R = MeCO, R' = MeCH–C(MeCO, epoxypterixin (Ref.58)
O
(CXIII) R = MeCO, R' = $MeCH_2CH(Me)CO$, dihydropterixin;
(CXIV) R = MeCH = C(Me)CO-*trans*, R' = MeCO, visnadin;
(CXV) R = Me_2CHCH_2CO, R' = MeCO, dihydrosamidin;
(CXVI) R = R' = MeCH = C(Me)CO-*trans*, anomalin (Ref.55);
(CXVII) R = MeCH = C(Me)CO-*trans*,
R' = MeCH—C(Me)CO;
O
(CXVIII) R = R' = MeCH—C(Me)CO (Ref.58);
O
(CXIX) R = MeCH = C(Me)CO-*trans*,
R' = MeSCH = CHCO, floroselin;
(CXX) R = MeCH = C(Me)CO-*trans*,
R' = Me, methanolysis of floroselin (Ref.55).

On the whole all the above compounds undergo the same types of decomposition on electron bombardment as do linear pyranochromenones.

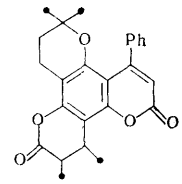
Mass spectra have been described also for several 4-phenylpyranochromen-2-ones with a different mode of fusion of the rings[15]



(CXXI) R = Me, R' = H;
(CXXII) R = Me, R' = MeCH = C(Me)CO-*trans*;
(CXXIII) R = MeCO, R' = $MeCH_2CH(Me)CO$ (Ref.15),



(CXXIV) R = H, R' = Me;
(CXXV) R = Me_2CHCH_2CO, R' = H (Ref.15),



(CXXVI)

as well as polyfunctional angular pyranochromenones isolated from *Mammea americana* L.[13] and *M. africana* G. Don.[40] Molecular ions of these compounds break down on electron bombardment similarly to the furochromenones and linear pyranochromenones described above.

Another type of angular pyranochromenone, in which the two pyran rings are fused together—4-methylpyrano-[5,6-*c*]chromen-2,5-dione (CXXVII)—was described by Johnstone et al.[10] Its mass spectrum represents a four-stage elimination of carbonyl groups and includes a metastable peak, indicating that the second and third carbonyls may be eliminated in a single stage. Such an observation is not unique, and has been reported in particular for monocyclic 2-pyrones. This simultaneous elimination of two carbonyl groups suggests that they may be contiguous. Measurement of the ionisation and appearance potentials at each stage, together with a study of the mass spectrum of the 5-carbon-13 analogue, made it possible to assess the sequence in which the carbonyl groups were ejected.

In order to elucidate the structure of the 200 ion $[M - CO]^+$ the mass spectrum of this pyranochromenone was compared with that of a similarly fused furochromenone. Although the spectra were qualitatively and quantitatively almost identical in the region of 200 and below, it was considered that these two 200 ions differed in structure, since the appearance potential of one differed appreciably from the ionisation potential of the other. An open-chain structure was therefore assigned to the 200 ion $[M - CO]^+$ in the case of the pyranochromenone (CXXVII). As has been stated earlier in connection with chromen-2-one itself, the Reviewers regard this conclusion as questionable.

Finally it must be emphasised that this Review makes no claim to exhaustive coverage of published information,

but nevertheless the Reviewers hope that it will show quite clearly the possibilities and limitations of mass spectrometry for determining the structure of naturally occurring chromen-2-ones, furochromenones, and pyranochromenones.

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Stabilisation of the Surface Potential and Determination of the Activities of Individual Ions in Solution

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The problem of the determination of the thermodynamic characteristics of individual ions, the Galvani potentials, and the liquid junction potentials by a method based on the stabilisation of the surface potentials of electrolyte solutions is examined. The results of experiments on the applications of surface-active agents (aliphatic carboxylic acids, alcohols and amines) as stabilisers of the surface potentials are discussed. The scope and limitations of the method are indicated. The bibliography includes 85 references.

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I. INTRODUCTION

The problem of determining the thermodynamic characteristics of individual ions and their variation with the composition of the medium still remains controversial in the physical chemistry of electrolyte solutions. The development of ideas in this field has been notably influenced by Guggenheim [1,2], who formulated the following principle: "the electrical potential difference between two points in different media can never be measured and has not yet been defined in terms of physical realities. It is therefore a conception which has no physical significance"[2]. From this point of view, the Galvani potential between the electrode and the electrolyte solution, the liquid junction potential (diffusion potential), and the potential difference between the gas phase (or vacuum) and a condensed phase (the surface or χ-potential) are not susceptible to experimental determination and lack physical significance. The above potential differences are functionally related to the activities and other thermodynamic characteristics of individual ions in solution (see, for example, Izmailov [3]). Thus the latter cannot be measured either and lack physical significance. Furthermore, according to Guggenheim there is no need for their determination, since the thermodynamic state of an electrolyte solution can be described in terms of the thermodynamic characteristics of the electrolyte as a whole or electrically neutral combinations of the charged components of the solution, which are susceptible to experimental determination.

Up to the present time, the majority of investigators have not shared Guggenheim's radical view, although the thesis that the thermodynamic characteristics of individual ions are not susceptible to the determination within the framework of rigorous thermodynamics appears to be generally accepted. The possibility, in principle, of measuring the potentials of individual electrodes was demonstrated in recent studies [4,5], although it has still not proved possible to develop experimental methods based on these ideas. The greatest progress has been achieved in the development of methods for the estimation of the thermodynamic characteristics of individual ions based on

different kinds of non-thermodynamic assumptions. The results obtained by these methods are discussed in a number of monographs [3,6,7] and reviews [8-10]. The available methods based on non-thermodynamic assumptions have been classified in the review by Popovych [8], who divides them into two categories. The first includes methods based on the estimation of the liquid junction potentials (Bjerrum and Larsson [11], Oiwa [12] and Parker and coworkers [13]) and the second includes methods involving correlations between the dimensions of ions and molecules and their solvation energies (Pleskov's normal cell method [14], Strehlow's ferrocene–ferricinium electrode method [15], Izmailov's extrapolation methods [16,17], Grunwald's standard electrolyte method [18], de Ligny's method [19], and others). Furthermore, Popovych considers in a separate category methods based on the estimation of Galvani potentials. The usefulness of these methods for the solution of the problem under discussion has been frequently noted [20]. This review deals with the problem of using the method based on the stabilisation of the χ-potentials of electrolyte solutions for the estimation of the activities of individual ions and the solvent effects for such ions and also to determine the Galvani potentials and liquid junction potentials.

II. PRINCIPLES OF THE SURFACE POTENTIAL STABILISATION METHOD

1. Calculation of the Thermodynamic Characteristics of Individual Ions from the Real Potentials of Ions and the Surface Potentials of Solvents

The principle of the calculation of the thermodynamic characteristics of individual ions in solution using the χ-potentials of the solvent was formulated after the development of the concept of the real potential† (real solvation energy) of ions α_i (Frumkin [22], Lange and Mishchenko [23]). According to Lange and Mishchenko [23], the real potential of ions α_i is related to their chemical potential (chemical solvation energy) μ_i as follows:

$$\alpha_i = \mu_i + z_i F\chi, \tag{1}$$

where z_i is the ionic charge and F the Faraday. The potentials α_i can be calculated directly from experimental data [24-27]. For ions in aqueous solutions, the most reliable data have been obtained by Randles [27], who estimates the error in the α_i for cations as ±0.5 kcal g-ion^{-1} and for anions as ±1 kcal g-ion^{-1}. The χ-potentials of solvents, which are defined as potential differences between points in different media, are inaccessible to direct measurements. Theoretical calculation of this quantity for water leads to an improbably high result [28]. Estimates of χ_{H_2O} based on non-thermodynamic assumptions have been frequently made [25,26,29-34]. The values of χ_{H_2O} obtained vary from −0.5 to 1.0 V. The low accuracy of the α_i and the uncertainty in χ for water and other solvents vitiate at present the attempts to obtain accurate values of $\lg \gamma_i^\circ$ (the so-called medium effects) or other corresponding thermodynamic characteristics of individual ions in terms of the absolute values of α_i.

†In defining the concepts of the electrochemical, real, and chemical potentials of ions, we follow the terminology employed by Parsons [21].

2. Non-thermodynamic Assumption of a Constant Surface Potential

It is easier to estimate the medium effects and the activities of individual ions in terms of the changes in the real and χ-potentials. Eqn. (1) can be transformed as follows:

$$\Delta\alpha_i = \Delta\mu_i + z_i F\,\Delta\chi, \tag{2}$$

where $\Delta\alpha_i$ is the change in the real potential of the ith ion and $\Delta\chi$ the change in surface potential on passing from one solution to another. It follows from Eqn. (2) that, when the surface potentials of solutions are stabilised (i.e. when $\Delta\chi = 0$), the values of $\Delta\alpha_i$ determined experimentally are equal to the corresponding changes in the chemical potential of ions of type i. Measurements of $\Delta\alpha_i$ on passing from one solvent to another have recently become common [36-41]. The experimental determination of $\Delta\alpha_i$ is based on the following factors. The real potential α_i is related to the electrochemical potential $\bar{\mu}_i$ by the familiar expression

$$\bar{\mu}_i = \alpha_i + z_i F\psi, \tag{3}$$

where ψ is the external potential of the phase. If two conducting phases whose interface is permeable only to charged species of type i are brought into electrical contact, the electrochemical potentials of such species in these phases become equal:

$$\bar{\mu}_i^{(1)} = \bar{\mu}_i^{(2)}\ . \tag{4}$$

Using Eqn. (3), one can write

$$\alpha_i^{(1)} + z_i F\psi^{(1)} = \alpha_i^{(2)} + z_i F\psi^{(2)}, \tag{5}$$

or

$$\Delta\psi = \psi^{(1)} - \psi^{(2)} = (\alpha_i^{(2)} - \alpha_i^{(1)})/z_i F = \Delta\alpha_i/z_i F, \tag{6}$$

where $\Delta\psi$ is the difference between the external potentials or the Volta potential difference arising between phases (1) and (2) as a result of the contact between them. Rabinovich [42] showed that more correctly the potential $\Delta\epsilon$, compensating $\Delta\psi$, is proportional to $\Delta\alpha_i$, rather than $\Delta\psi$ itself, since at the instant of compensation the phases are subjected to the same potential relative to earth and therefore there is no need for the assumption that the real potential is independent of the charge of the phase (Bridgman's hypothesis [43]). Henceforth, we shall call $\Delta\epsilon$ the "compensating potential"‡. Consequently, one can write

$$\Delta\varepsilon = \Delta\alpha_i/z_i F. \tag{7}$$

The interfaces between electrolyte solutions are permeable to both cations and anions. Nevertheless, systems permeable to ions of only one type can be produced by means of reversible ion-selective electrodes. We shall consider the specific instance of solutions of a strong acid HA for which it is necessary to determine the thermodynamic state of H^+ ions. Isolated HA solutions in which two reversible hydrogen electrodes are immersed and which are joined by a metallic conductor constitute a system permeable to H^+ ions only (Fig. 1*a*). One of the HA solutions will be regarded as the standard and the

‡The condenser and ionisation methods as well as flow methods are equally suitable for the measurement of $\Delta\epsilon$. Kenrick's method [44] has been widely used hitherto for the determination of $\Delta\alpha_i$. The technique of the measurements has been described in detail [45].

other as the test solution. As a result of contacts via the hydrogen electrodes, the previously electrically neutral HA solutions are charged relative to one another and a Volta potential difference arises between their free surfaces. The contact charging of solution is due to the fact that, by virtue of the difference between their compositions, the electrochemical potentials of the H^+ ions in them are different too. By virtue of the equilibrium $H^+ + e \rightleftharpoons \frac{1}{2}H_2$ between the solution and the electrodes, the electrochemical potentials $\bar{\mu}_e$ of the electrons in the solid phase of the electrodes should also be different. Contact between the hydrogen electrodes leads to the equalisation of the $\bar{\mu}_e$, which shifts the equilibrium $H^+ + e \rightleftharpoons \frac{1}{2}H_2$. As a result, a number of H^+ ions disappear from the HA solution where their activity is higher and an equal number appear in the solution where their activity is lower. The compensating potential $\Delta\epsilon$ which shifts the equilibrium in the system so that the Volta potential difference $\Delta\psi$ between the solutions becomes zero can be selected by means of a potentiometer included in the circuit between the hydrogen electrodes (Fig. 1*b*). For the given specific case, Eqn. (7) becomes

$$\Delta\varepsilon = [\alpha_{H^+}(m) - \alpha_{H^+}(m_{st})]/F, \qquad (8)$$

where $\alpha_{H^+}(m)$ and $\alpha_{H^+}(m_{st})$ are the real potentials of H^+ ions in the test and standard solutions respectively. The electrochemical system illustrated in Fig. 1*a* is usually represented symbolically as follows:

$$\mathrm{Pt(H_2)}\,|\,\mathrm{HA},\ m_2\,|\,\mathrm{air}\,|\,\mathrm{HA},\ m_{st}\,|\,\mathrm{Pt(H_2)}. \qquad (A)$$

In contrast to the usual galvanic cells, such systems will be called Voltaic cells.

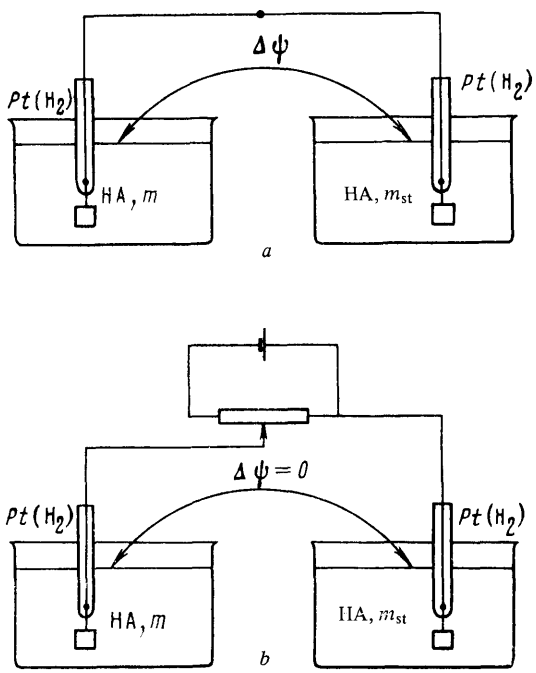

Figure 1. Schematic illustration of the electrochemical system used to investigate the Volta effect on joining together two electrolyte solutions via ion-selective electrodes: *a*) contact charging of the solutions; *b*) compensation of the Volta potential difference produced using a potentiometer to generate a compensating potential.

According to Eqns. (2) and (7), the compensating potential of the voltaic cell (A) is proportional to the difference between the chemical potentials of H^+ ions in the test and standard solutions when the difference between the potentials jumps at the interfaces *2* and *3* in the cell is zero ($\Delta\chi = 0$). This condition holds when the solutions being compared are fairly dilute or when their surface potentials are artificially stabilised. With the aid of the voltaic cell (A), it is in essence possible to determine $\mu_{H^+} - \mu^\circ_{H^+}$ to within the unknown value of $F\Delta\chi$.

The assumption that $F\Delta\chi$ is zero implies the non-thermodynamic assumption of the equality of the surface potentials of the solutions being compared. In practice, it is more convenient to employ, instead of a voltaic cell of type (A), a voltaic cell of the following type:

$$\mathrm{Pt(H_2)}\,|\,\mathrm{HA},\ m\,|\,\mathrm{air}\,|\,\text{standard solution}\,|\,\text{reference electrode}, \qquad (A')$$

the $\Delta\epsilon$ values for which can be readily converted into the $\Delta\epsilon$ value for a cell of type (A) by a computational procedure.

On the basis of the non-thermodynamic assumption of equal surface potentials, a voltaic cell of type (A) essentially permits an experimental determination of the dependence of the Galvani potentials of the individual electrodes on the composition of the electrolyte solution. A similar relation for the liquid junction potentials permits a determination for voltaic cells of the type

$$\mathrm{Hg}\,|\,\mathrm{Hg_2Cl_2}\,|\,\text{saturated KCl solution}\,|\,\mathrm{HA},\ m\,|\,\mathrm{air}\,|\,\text{standard solution}\,|\,\text{reference electrode}. \qquad (B)$$

Indeed if the potential jump at the interface between the HA solution and air does not vary with the composition of the solution, the change $\Delta\epsilon$ for a voltaic cell of type (B) is due exclusively to the change in the liquid junction potential ΔE_j at the interface between the HA solution and the saturated KCl solution.

3. The Concepts of the "Real" Ionic Activity and the "Real" Acidity of the Medium

For further exposition, it is important to consider the concepts of the "real" ionic acitivity in solution[46] and the "real" acidity of the medium[47]. The activities of individual ions in solution a_i as well as the activities of the electrically neutral components are usually defined by the equation

$$\mu_i = \mu_i^\circ + RT\ln a_i = \mu_i^\circ + RT\ln m_i\gamma_i, \qquad (9)$$

where μ_i° is the chemical potential of ions of type i in the standard state, γ_i their chemical activity coefficient in the test solution, and m_i their molality. However, a physical interpretation of Eqn. (9) is difficult, because it is impossible to imagine a real transfer of the charged solution component from the standard state to the test solution without crossing the interface. Rabinovich et al.[46] suggested that the thermodynamic activities of ions in solution be defined by the equation

$$a_i = a_i^\circ + RT\ln a_i^r = a_i^\circ + RT\ln m_i\gamma_i^r, \qquad (10)$$

where m_i, a_i^r, and γ_i^r are the molality, real activity, and real activity coefficient of species of type i respectively. In the special case of H^+ ions the quantity $-\ln a^r_{H^+} = pa^r_H$ will be called the real acidity of the solution (medium). The following real physical process corresponds to Eqn. (10): the transfer of one gramme-ion of charged species of type i from the electrically neutral test phase to the standard phase (Fig. 2). The ions pass from the test

phase to a point in the gas phase (or *in vacuo*) at an infinite distance from the test phase, crossing the boundary between the test phase and air; in this process they overcome the energy barrier due to the electrical double layer at this boundary, which is characterised by the χ-potential of the phase. In such a transition it is necessary to expend work equal to the real solvation energy of species of types i in the test phase. Next the ions pass from the gas phase to the standard phase, also crossing (this time in the opposite direction) the corresponding interface. This transition involves a gain in work equal to the real solvation energy of species of type i in the standard phase. Thus the quantities a_i^r and γ_i^r are measures of the change in the real solvation energy (real potential) of the charged species on passing from the standard state to the test solution. If the transfer process proceeds under the conditions of equal surface potentials of the phases ($\Delta\chi = 0$), then, according to Eqns. (2) and (9), the real activity and activity coefficient are equal to the corresponding chemical quantities.

We shall employ the same formal treatment for the real activities and activity coefficients of ions as for the mean ionic activities and activity coefficients of electrolytes. The overall real activity coefficient γ_i^r becomes unity only at infinite dilution in aqueous solution. For the test solvent, γ_i^r tends to a limiting value $\gamma_i^{r\circ}$ when $m_i \to 0$. We shall call this value the real solvent activity coefficient. The activity coefficients γ_i^r and $\gamma_i^{r\circ}$ are linked by the relation

$$\gamma_i^r = \gamma_i^{r*}\gamma_i^{r\circ}. \qquad (11)$$

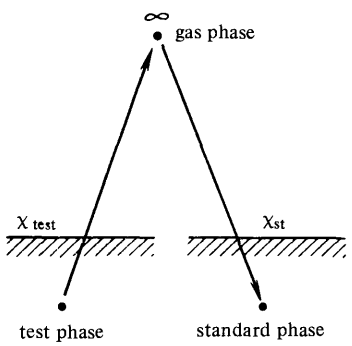

Figure 2. Schematic illustration of the transfer of the charged component of the electrolyte solution from the test phase to the standard phase via the gas phase.

The coefficient γ_i^{r*}, which we shall call the real concentration activity coefficient, becomes unity at infinite dilution in the given solvent. Finally, the product of the real activity coefficients of the electrolyte ions is equal to the square of the mean ionic activity coefficient:

$$\gamma_+^r\gamma_-^r = \gamma_\pm^2. \qquad (12)$$

The activity coefficients $\gamma_\pm$, $\gamma_\pm^*$, and $\gamma_\pm^\circ$ are usually called the overall, salt, and solvent effects of the medium respectively. However, this terminology is inapplicable to real activity coefficients, since their numerical values, obtained from experimental data, depend not only on the state of the ions in the bulk of the solution but also on the electrical states of the surfaces of the solutions being compared. Only when the experiment is carried out under the conditions of equal χ-potentials of the solutions being compared can the real activity coefficients be interpreted as medium effects for the individual ions.

III. DISCUSSION OF EXPERIMENTAL RESULTS OBTAINED BY THE SURFACE POTENTIAL STABILISATION METHOD

The stabilisation of the χ-potential by surface-active substances was observed[48] for HCl solutions. The authors determined the real activity coefficients of H^+ and Cl^- ions in aqueous and aqueous alcoholic HCl solutions by measuring the compensating potentials of the voltaic cell

$$Ag \mid AgCl \mid HCl, m \mid air \mid KCl, m_{st} \mid AgCl \mid Ag,$$

and the electrical potentials of the galvanic cells

$$Pt(H_2) \mid HCl, m \mid AgCl \mid Ag.$$

It was found that the values of $\gamma_{H^+}^{r*}$ and $\gamma_{Cl^-}^{r*}$, which differ sharply from one another and from the $\gamma_\pm^*$ in pure HCl solutions, approach one another and almost coincide with the $\gamma_\pm^*$ for solutions to which 1% of n-pentyl alcohol has been added (Table 1). This was given the following explanation, which subsequent studies showed to be inaccurate. Molecules of n-pentyl alcohol, which have a higher adsorption potential at the solution–air interface, displace the ions and undissociated HCl molecules from the surface layer of the solution, as a result of which the electrical properties of the surfaces of the HCl solutions become the same for different compositions.

Table 1. The real activity coefficients of H^+ and Cl^- ions in pure aqueous HCl solutions (*a*) and in HCl solutions containing 1% of n-pentyl alcohol (*b*) at 25°C.

HCl, M	*a*		*b*		*a*
	$\gamma_{H^+}^{r*}$	$\gamma_{Cl^-}^{r*}$	$\gamma_{H^+}^{r*}$	$\gamma_{Cl^-}^{r*}$	$\gamma_\pm^*$
0.01	0.82	0.99	0.90	0.94	0.90
0.02	0.79	0.98	0.87	0.92	0.88
0.05	0.74	0.94	0.82	0.88	0.83
0.10	0.70	0.89	0.78	0.86	0.80
0.20	0.71	0.82	0.73	0.85	0.77
0.50	0.98	0.59	0.72	0.85	0.76

The observed stabilisation of the χ-potentials of aqueous HCl solutions was then used[49] to determine the acidity of the medium in the HCl–H_2O system over the complete range of compositions. Voltaic cells of type (A′) were used for the measurements. The HCl–H_2O mixtures investigated were saturated with surface-active alcohols and aliphatic acids. The authors observed that the experimental real acidities pa_H^r of the solutions stabilised by heptyl and nonyl alcohols agreed with the corresponding Hammett acidity functions H_0,[50] while the pa_H^r for pure HCl solutions differed sharply from the H_0 (Table 2). Table 2 shows that significant discrepancies between pa_H^r and H_0 for solutions with heptyl alcohol are observed for concentrations of 12 M and above and for solutions saturated with n-nonyl alcohol for concentrations of 14 M and above. The mutual approach of the

values of pa_H^r and H_0 was explained by the complete equalisation of the χ-potentials of the HCl solutions when the latter were saturated with a surface-active agent, whose molecules displaced the electrolyte (HCl) from the surface layer. The agreement between the acidities of the medium obtained by fundamentally different methods is itself remarkable if one recalls that more than 10 different indicator acidity scales[51] are known at present for the H_2SO_4–H_2O, $HClO_4$–H_2O, and HCl–H_2O systems, which do not agree. This provides some justification for the interpretation of both the pa_H^r and H_0 values for HCl solutions as the protic activities of the medium pa_H.

Table 2. Comparison of the acidity functions for HCl–H_2O solutions on the basis of the results of Rybkin and Shevchenko[49].

Molality of HCl	pa_H^r			$-H_0^*$ (pure HCl soln.)
	pure HCl soln.	HCl soln. satd. with n-heptyl alcohol	HCl soln. satd. with n-nonyl alcohol	
0.5	−0.25	−0.26	−0.30	−0.28
1.0	0.36	0.13	0.11	0.07
2.0	1.30	0.50	0.50	0.50
3.0	2.16	0.81	0.81	0.83
4.0	2.96	1.12	1.14	1.15
5.0	3.73	1.47	1.47	1.48
6.0	4.45	1.75	1.75	1.77
7.0	5.23	2.06	2.03	2.06
8.0	6.05	2.35	2.34	2.36
10.0	7.37	2.92	2.89	2.88
12.0	8.75	3.50	3.40	3.37
14.0	9.90	4.16	4.01	3.86
16.0	10.91	4.85	4.65	4.35

*According to the results of Vinnik et al.[50]

The study of the stabilisation of the χ-potentials of solutions of strong inorganic acids was continued in another investigation[52], where the χ-potential shifts for the HCl solutions at different concentrations under the influence of surface-active alcohols were determined with the aid of a voltaic cell of type (B). Figs. 3 and 4 and Table 3 illustrate the results of this study in relation to the χ-potential shifts due to the adsorption of n-heptyl and n-perfluoroheptyl alcohols. Whereas the χ-potential shift on passing from pure 0.1 M HCl solution to the corresponding HCl solution saturated with n-heptyl alcohol is about 300 mV, the shift for the 15 M HCl solution is about 550 mV.

This was explained[52] by the fact that in concentrated HCl solutions the formation of a monolayer of the surface-active alcohol at the solution–air interface is accompanied by the disruption of the double layer due to the adsorption of HCl. Another explanation is also possible. The monolayer of the surface-active molecules screens the adsorption layer formed by the HCl dipoles, as a result of which the latter does not influence the external potential of the solution. Therefore, when HCl solutions are saturated with a surface-active alcohol, their χ-potentials are determined only by the monolayer of the surface-active molecules, regardless of the HCl concentration, and are therefore the same for all HCl solutions. Since the adsorption of n-heptyl alcohol and of HCl shift the χ-potential of water in opposite directions, these effects are combined and the overall shift of the χ-potentials of concentrated HCl solutions is large.

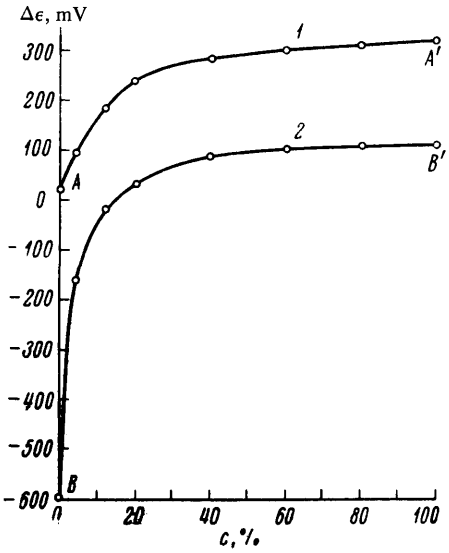

Figure 3. The adsorption shift of the χ-potentials of HCl solutions following their saturation with n-heptyl alcohol [1) 0.32 M HCl; 2) 16.42 M HCl]. The concentration c of the surface-active agent, expressed as a percentage relative to its concentration in the saturated solution, is plotted as abscissa.

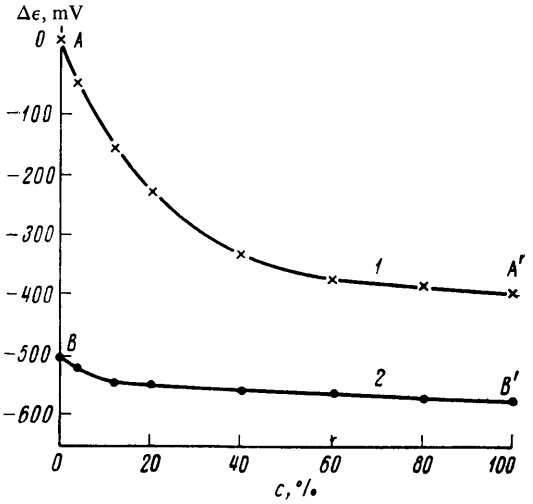

Figure 4. Adsorption shift of the χ-potentials of HCl solutions following their saturation with n-perfluoroheptyl alcohol [1) 0.3 M HCl; 2) 14.7 M HCl]. The concentration c of the surface-active agent, expressed as a percentage relative to its concentration in the saturated solution, is plotted as abscissa.

In conformity with the foregoing considerations, the lengths of the $A'B'$ sections in Figs. 3 and 4 can be interpreted as representing the change in the compensating potential of a cell of type (B) caused exclusively by the change in the liquid junction potential ΔE_j at the interfaces between the test solutions and the saturated KCl

solution as the HCl concentration is varied. The lengths of the *AB* sections in these figures reflect the changes in $\Delta\epsilon$ for a cell of type (B) caused both by the shift of the χ-potential of water following the adsorption of HCl at the solution–air interface and by ΔE_j as the HCl concentration is varied. If it is assumed that the ΔE_j are independent of the presence of the surface-active agent in the HCl solutions, it is easy to calculate the change in the adsorption potential of hydrochloric acid ΔE_{HCl} at the solution–air interface with change in the HCl concentration. The adsorption potential of HCl (ΔE_{HCl}) is understood as the component of $\Delta\epsilon$ for a voltaic cell of type (B) due to the adsorption of HCl alone at the solution–air interface. The numerical values of ΔE_{HCl} are equal to the lengths of the *AB* and *A'B'* sections and are listed in Table 3.

Table 3. The acidity functions pa_H^r and H_0, the HCl adsorption potentials, the liquid junction potentials in cell (B), and the compensating potentials in cell (B) for aqueous HCl solutions at 25°C.

HCl, mole %	$-pa_H^r$		$-H_0$	ΔE_{HA}^{**}, mV	ΔE_j*, mV	$\Delta\epsilon$***, mV
	pure solns.	stabilised solns.*				
1	−0.10	−0.14	−0.13	12	2	14
2	0.52	0.24	0.27	22	6	28
3	1.08	0.49	0.51	35	10	45
4	1.56	0.71	0.74	50	16	66
5	2.00	0.92	0.96	64	23	87
6	2.55	1.14	1.16	83	28	111
7	3.08	1.36	1.36	102	35	137
8	3.60	1.58	1.57	119	45	164
9	4.13	1.80	1.76	138	53	191
10	4.60	2.01	1.94	153	67	220
12	5.74	2.44	2.20	195	82	277
14	6.83	2.85	2.68	235	95	330
16	7.90	3.24	3.07	276	114	390
18	8.90	3.62	3.44	312	141	453
20	9.83	3.98	3.80	346	169	515
22	10.73	4.30	4.14	380	197	577

*Averaged for solns. stabilised with n-heptyl, n-perfluoroheptyl and isopentyl alcohols.

**The positive sign ΔE_j, ΔE_{HA}, and $\Delta\epsilon$ implies that the reference electrode in a cell of type (B), immersed in the standard solution, becomes more positive owing to these potential shifts relative to the calomel electrode in the test solution.

***Referred to the compensating potential of a cell of type (B) for pure 0.01 M HCl solution.

The curves in Fig. 4 represent the χ-potential shifts for HCl solutions under the influence of n-perfluoroheptyl alcohol, which displaces the potential of water in the same direction as that of HCl. Therefore, the overall shift of the χ-potential diminishes with increase of HCl concentration and it may happen that in concentrated HCl solutions the surface activity of n-perfluoroheptyl alcohol is reduced. It is interesting that, when n-heptyl and n-perfluoroheptyl alcohols are used, similar values of ΔE_j and ΔE_{HCl} are obtained. Figs. 3 and 4 also show that the "tail" sections of the curves relating $\Delta\epsilon$ to the concentration of the surface-active agent are almost parallel.

When the variation of ΔE_{HCl} with the concentration of the surface-active agent is determined, it is found that, at a relative concentration of n-heptyl alcohol of 4%, the adsorption potential ΔE_{HCl} is already close to zero.

Thus, at comparatively low concentrations of the surface-active agent, the electrical properties of the surfaces of the solutions already approach those of the surface of the solution saturated with the surface-active alcohol. As before[49], the values of pa_H^r found from the observed ΔE_j and the experimental data for the cells with transport

$$Pt(H_2)\,|\,HCl,\ m\,|\,\text{sat. KCl soln.}\,|\,\text{reference electrode}\ \S$$

proved to be extremely close to the corresponding acidity functions H_0.[53]

The results of experiments on the stabilisation of the χ-potentials of concentrated HBr and $HClO_4$ solutions have been published[54]. Calculation of pa_H^r for HBr solutions from experimental data for cells of types (B) and (B') on the assumption that the surface-active agent (n-heptyl alcohol) causes the complete equalisation of the χ-potentials of the HBr solutions leads to values which differ appreciably from the corresponding acidity functions H_0 [55] (Table 4). This result can be explained by the fact that n-heptyl alcohol only partially stabilises the χ-potentials of HBr solutions. The monolayer of n-heptyl alcohol molecules, screening the adsorption layer of HBr dipoles, cannot constitute an obstacle to the electrostatic field generated by the Br^- ions which have undergone specific adsorption at the solution–air interface.

Table 4. The acidity functions pa_H^r and H_0, the adsorption potentials ΔE_{HA} and ΔE_{A^-}, the changes in the liquid junction potential ΔE_j in cell (B), and the compensating potentials $\Delta\epsilon$ in cell (B) for $HBr–H_2O$ solutions at 25°C.

HBr, mole %	$-pa_H^r$			$-H_0$	ΔE_{HA}, mV	ΔE_{A^-}, mV	ΔE_j, mV	$\Delta\epsilon$, mV
	pure solns.	solns. satd. with surface-active agent	with allowance for ΔE_{A^-}					
1	−0.09	−0.22	−0.32	−0.32	8	5	5	18
2	0.66	0.32	0.18	0.15	20	9	8	37
3	1.25	0.69	0.46	0.42	33	13	15	61
4	1.81	1.03	0.72	0.67	46	18	21	85
5	2.39	1.38	0.99	0.89	60	23	28	111
6	3.00	1.77	1.24	1.09	73	31	35	141
7	3.57	2.10	1.45	1.28	87	37	40	164
8	4.13	2.42	1.62	1.49	101	44	41	186
9	4.72	2.76	1.79	1.69	116	57	41	214
10	5.31	3.10	1.94	1.92	131	69	40	240
11	5.95	3.48	2.12	2.13	146	—	—	270
12	6.60	3.84	—	2.34	163	—	—	295
13	7.24	4.21	—	2.58	179	—	—	322
14	7.93	4.63	—	2.83	195	—	—	354
15	8.60	5.02	—	3.06	212	—	—	384
16	9.34	5.47	—	—	229	—	—	415

Accordingly, the χ-potential shift can be expressed as a function of HBr concentration in the form of a sum of the changes of two components: the adsorption potential due to the adsorbed undissociated HBr molecules (ΔE_{HBr}) and the adsorption potential due to the specifically adsorbed Br^- ions (ΔE_{Br^-}). The values of ΔE_{Br^-} can be estimated approximately from the χ-potential shift for water[56] under the influence of metal bromides, obtained with the aid of a voltaic cell of the type

$$Hg\,|\,Hg_2Cl_2\,|\,\text{sat. KCl. soln.}\,|\,MBr\,|\,\text{air}\,|\,\text{reference soln.}\,|\,\text{reference electrode.}\ \S$$

§Cell (B')? (Ed. of Translation).

Although the estimate of ΔE_{Br^-} for HBr solutions involves at least two gross assumptions (namely that the degrees of dissociation of HBr and metal bromides MBr are the same in equimolar solutions and that the liquid junction potentials in the above voltaic cell does not vary with MBr concentration), allowance for ΔE_{Br^-} in the calculation of pa_H^r from experimental data leads to satisfactory agreement between pa_H^r and the values of H_0, as can be seen from the data in Table 4. The results obtained for $HClO_4$ solutions were exactly the same (Table 5).

Table 5. The acidity functions pa_H^r and H_0, the adsorption potentials ΔE_{HA} and ΔE_{A^-}, the changes in the liquid junction potential ΔE_j in cell (B), and the compensating potentials $\Delta\epsilon$ in cell (B) for $HClO_4$–H_2O solutions at 25°C.

HA, mole %	$-pa_H^r$			$-H_0$	ΔE_{HA}, mV	ΔE_{A^-}, mV	ΔE_j, mV	$\Delta\epsilon$, mV
	pure solns.	solns. satd. with surface-active agent	with allowance for ΔE_{A^-}					
1	−0.10	−0.20	−0.20	−0.20	5	4	20	29
2	0.90	0.60	0.36	0.40	16	14	35	65
3	1.60	1.15	0.72	0.68	26	25	42	93
4	2.20	1.55	0.96	0.92	38	35	48	121
5	2.80	1.98	1.20	1.16	50	45	51	146
6	3.40	2.38	1.41	1.40	63	55	55	173
7	4.00	2.72	1.61	1.63	76	66	60	202
8	4.50	3.03	1.74	1.83	89	76	63	228
9	5.05	3.35	1.84	2.04	102	88	68	258
10	5.65	3.70	2.03	2.26	115	100	73	288
11	6.25	4.10	2.30	2.49	128	112	79	319
12	6.85	4.48	—	2.74	141	—	—	—
13	7.45	4.82	—	2.97	154	—	—	—
14	8.00	5.16	—	3.22	168	—	—	—
15	8.60	525.	—	3.47	183	—	—	—
16	9.20	5.85	—	3.73	—	—	—	—
17	9.75	6.18	—	3.99	—	—	—	—
18	10.40	6.50	—	4.25	—	—	—	—
19	11.00	6.83	—	4.55	—	—	—	—
20	11.65	7.23	—	4.86	—	—	—	—

Commenting on the results described[52,54], the following factors should be noted. The complete stabilisation of the χ-potential by non-ionogenic surface-active substances (particularly aliphatic alcohols) can be achieved only when there is no specific adsorption of the charged solution components and charged monolayers are not formed on the free solution surface. The question of the stabilisation of the surface potentials of solutions on the free surfaces of which charged species are specifically adsorbed remains open and its further investigation is extremely desirable. Furthermore, the changes $\Delta\epsilon$ for voltaic cells of type (B) as the acid concentration is varied can be divided into three components corresponding to the changes in the liquid junction potential ΔE_j, the adsorption potential ΔE_{HA} due to the molecular adsorption of acids and the adsorption potential ΔE_{A^-} due to the specific adsorption of the acid anions.

The results[52,54] yielded new information about the structure of the surfaces of solutions of strong inorganic acids. To explain the anomalously high adsorption shift of the χ-potential caused by strong acids, Randles suggested that H_3O^+ ions in the surface layer are preferentially oriented with the three H atoms directed towards the liquid phase. He believes that the other possible explanation, involving the preferential orientation of the ion pairs or undissociated acid molecules near the surface is unlikely, since $HClO_4$ and HI cause the greatest shifts of the χ-potential, while the dipole moments of these acids are smaller than that of HCl. The results presented in Tables 3, 4 and 5 show that, although $\Delta\epsilon$ for a cell of type (B) does decrease in the sequence $HClO_4 > HBr > HCl$, the quantity ΔE_{HA} increases in this sequence, which agrees with the increase in the dipole moments of the molecules on passing from HBr to HCl (the dipole moments of $HClO_4$ molecules are not available). Thus the experimental results support the hypothesis of the preferential orientation of the undissociated acid molecules in the surface layer.

The fact that the adsorption potentials of acids can be divided into molecular and ionic components (ΔE_{HA} and ΔE_{A^-}) using experimental data (on the basis of the non-thermodynamic assumption of the equality of the surface potentials of the stabilised solutions) suggests that the surface layers of solutions of strong acids consist of two sublayers. The upper sublayer adjoining the gas phase contains undissociated acid molecules with a preferential orientation of the dipoles such that the negative poles point towards the gas phase. These molecules may be hydrated. Ion pairs separated by solvent molecules are located in the lower sublayer with the same orientation of the dipoles. The monolayer of molecules of the surface-active agent on the solution–air interface screens the field generated by the acid and solvent dipoles in the upper sublayer. However, this sublayer does not constitute an obstacle to the electrostatic field generated by the ion pairs.

Table 6. The acidity functions pH, pa_H^r, and H_-, the adsorption potentials, the liquid junction potentials in cell (B), and the compensating potentials $\Delta\epsilon$ in cell (B) for NH_3–H_2O and N_2H_4–H_2O solutions at 25°C.

Concentration	$NH_3 - H_2O$					$N_2H_4 - H_2O$					
	pH	pa_H^r	$\Delta\epsilon$	ΔE_j	ΔE_{NH_3}	pH	pa_H^r	H_-	$\Delta\epsilon$	ΔE_j	$\Delta E_{N_2H_4}$
0.01	9.90	9.90	0	0	0	9.26	9.26	—	—	0	0
0.05	10.50	10.50	2	0	2	9.83	9.82	—	0	−1	1
0.1	10.74	10.74	8	0	8	10.09	10.07	—	1	−2	3
0.5	11.39	11.42	38	1	37	10.67	10.60	—	6	−5	11
1.0	11.60	11.65	75	3	72	10.94	10.84	—	17	−8	25
2.0	11.86	11.94	118	6	112	11.18	11.03	—	41	−9	50
3.0	12.00	12.14	155	9	146	11.42	11.25	—	65	−9	74
4.0	12.13	12.30	192	11	181	11.66	11.51	10.87	93	−8	101
5.0	12.24	12.47	217	14	203	11.86	11.73	11.45	114	−7	121
6.0	12.35	12.63	241	17	224	12.05	11.95	11.95	139	−6	145
7.0	12.47	12.79	262	20	242	12.25	12.17	12.42	162	−5	167
8.0	12.58	12.95	280	23	257	12.44	12.39	12.87	185	−3	188
10.0	12.80	13.27	313	27	286	12.79	12.87	13.55	228	+2	226
12.0	13.00	13.59	349	34	315	13.12	13.27	14.12	270	7	263
14.0	—	—	—	—	—	13.40	13.65	14.55	302	14	288
16.0	—	—	—	—	—	13.75	14.05	—	328	20	308
18.0	—	—	—	—	—	14.10	14.50	—	352	24	328

The stabilisation of the surface potentials of concentrated NH_3 and N_2H_4 solutions has been investigated[58,59] by the method used by Rybkin and Karpenko[52]. The surface-active agents employed were isopentyl and hexyl alcohols, hexylamine, and 1,1,3-tetramethylbutylamine. The use of these agents leads to similar values of ΔE_j and pa_H^r (Table 6). ΔE_j for NH_3–H_2O solutions does not vary greatly (only by 35 mV on passing from dilute solutions to 12 M NH_3 solution). Therefore, the real acidities of these media differ little from the pH. There are no literature values of the acidity functions H_0 or H_- for NH_3–H_2O solutions, which precludes a comparison of the results of the electrometric and indicator methods for the measurement of the acidity of the medium.

Table 7. The H_-, pH, and pa_H^r basicity scales for aqueous lithium, sodium, and potassium hydroxide solutions at 25°C.

Concn. of alkali, M	LiOH					NaOH					KOH			
	H_-^{61}	H_-^{62}	H_-^{63}	pH	pa_H^r	H_-^{61}	H_-^{64}	H_-^{65}	pH	pa_H^r	H_-^{61}	H_-^{64}	pH	pa_H^r
0.1	—	—	—	12.82	12.82	12.99	—	13.01	12.80	12.88	13.00	—	12.90	12.90
0.5	13.68	—	—	13.37	13.37	13.71	—	13.71	13.45	13.53	13.75	—	13.50	13.47
1.0	13.96	13.85	13.48	13.60	13.67	14.02	14.00	14.01	13.71	13.76	14.11	14.00	13.81	13.76
2.0	14.26	14.23	13.66	13.81	13.84	14.37	14.36	14.40	14.00	14.00	14.51	14.49	14.18	14.08
3.0	14.45	14.47	13.87	13.92	13.91	14.65	14.64	14.66	14.18	14.10	14.85	14.87	14.46	14.31
4.0	14.58	14.63	14.10	14.00	13.97	14.95	14.93	14.87	14.33	14.13	15.15	15.12	14.67	14.46
5.0	—	14.75	14.33	14.08	14.07	15.20	15.14	—	14.45	14.10	15.44	15.45	14.88	14.61
6.0	—	—	—	—	—	15.40	15.37	15.31	14.57	14.07	15.72	15.74	15.10	14.77
7.0	—	—	—	—	—	15.62	15.58	—	14.68	14.04	16.00	16.07	15.30	14.93

The ΔE_j for N_2H_4–H_2O solutions are negative at low concentrations, but their sign changes at concentrations above 10 M. As in NH_3–H_2O solutions, ΔE_j does not reach high values (about 25 mV in the 20 M solution), as a result of which the values of pa_H^r and pH are similar. However, they differ somewhat from the H_-.[60] The authors do not give a preference for any one of these acidity scales. Nevertheless, bearing in mind the results of Rybkin and Karpenko[54], the following remarks may be made. NH_3 and N_2H_4 solutions are extremely convenient for applying the method based on the stabilisation of the surface potential, since the ionisation of ammonia and hydrazine in the bulk of the solution and hence in the surface layer is insignificant. Because of this, it is extremely likely that the surface potentials of these solutions are completely equalised when they are saturated by surface-active agents. It also permits the assertion that the pa_H^r scale reflects most satisfactorily the concentration dependence of the acidity of the medium for the NH_3–H_2O and N_2H_4–H_2O systems.

The study of the stabilisation of the surface potentials of concentrated lithium, sodium, and potassium hydroxide solutions[59] yielded less clear-cut results owing to experimental difficulties caused by the salting-out of the surface-active substances in concentrated solutions of alkalis and by the poor wetting of the glass by the solutions saturated with the surface-active agent. Nevertheless, experiment showed that the shift of the χ-potential following the addition of the surface-active agents to the solutions of alkalis decreases in absolute magnitude with increased concentration of alkali. This indicates the stabilisation of the surface potentials of these solutions and presumably the stabilisation is fairly satisfactory, since OH^- ions show a smaller tendency towards specific adsorption at the solution–air interface compared with other ions. Furthermore, the adsorption of OH^- ions should be compensated to some extent by the specific adsorption of the cations. Comparison of the pa_H^r and pH scales with the known values of H_- [61–65] for concentrated lithium, sodium, and potassium hydroxide solutions (Table 7) shows that the indicator method yields unduly high values of the basicity of the medium. However, the insufficiency of experimental acidity data and the experimental difficulties in the study of the stabilisation of the χ-potentials of these media make it so far impossible to give preference to any of the acidity scales mentioned above.

The stabilisation of the χ-potential of the HCOOH–H_2O system has been studied[66,67] by means of a voltaic cell of type (A′). Caproic and oenanthic acids were used as surface-active agents, because the employment of alcohols is undesirable owing to the possible formation of esters. Like the NH_3 and N_2H_4 solutions, HCOOH–H_2O mixtures are suitable for the application of the surface potential stabilisation method, since HCOOH is a moderately strong acid and therefore the specific adsorption of anions in the surface layer should be significant. A constant amount of added caproic and oenanthic acids (0.1 and 0.03 mole % respectively) stabilises the χ-potentials of the HCOOH–H_2O mixtures, as shown by the markedly different acidity functions pa_H^r obtained for the pure HCOOH–H_2O mixtures and for the same mixtures containing the surface-active agent (Table 8). Table 8 also lists the acidity functions H_0 [68] and the pH. The results in Table 8 show that the pa_H^r differ sharply from the corresponding values of the other functions, indicating a higher acidity of the medium than that given by the other functions.

Table 8. The acidity functions pa_H^r, pH, and H_0, the compensating potentials in cell (B), the adsorption potentials of formic acid, and the liquid junction potentials in cell (B) for HCOOH–H_2O solutions at 25°C.

HCOOH, mole %	$-pa_H^r$		−pH	$-H_0^*$	Δε, mV	ΔE_{HA}, mV	ΔE_j, mV
	pure HCOOH solns.	solns. satd. with surface-active agent					
0.5	−2.14	−2.14	−2.15	—	−1	0	−1
5.0	−0.78	−0.74	−1.47	−1.49	−41	3	−43
10.0	−0.22	0.63	−1.13	−1.39	−54	50	−104
15.0	0.18	1.98	−0.88	−1.13	−60	107	−167
20.0	0.62	3.22	−0.54	−0.98	−68	154	−222
25.0	0.96	4.30	−0.26	−0.85	−72	198	−270
30.0	1.22	5.22	0.00	−0.70	−72	237	−309
40.0	1.63	6.59	0.47	−0.43	−69	294	−362
50.0	1.96	7.42	0.89	−0.14	−63	323	−386
60.0	2.34	7.91	1.32	+0.19	−61	329	−390
70.0	2.81	8.28	1.77	0.50	−62	323	−385
80.0	3.41	8.76	2.30	0.84	−66	316	−382
90.0	4.12	9.49	2.92	1.22	−72	317	−389
100	4.89	10.47	3.67	2.19	−72	330	−402

*Interpolated from literature data[68].

The following comments may be made concerning Table 8. The known values[69] of the adsorption shift of the χ-potentials of water caused by aliphatic carboxylic acids (ranging from formic to caproic) are listed without correction for the change in the liquid junction potential in a cell of type (B). These data create the impression of an anomalous behaviour of formic acid, the addition of which

to water causes a negative shift of the χ-potential [negative values of $\Delta\epsilon$ for a cell of type (B) in Table 8], while the addition of the remaining acids of the same homologous series leads to a corresponding shift in the opposite direction. The results[66,67] compiled in Table 8 show that the adsorption behaviour of formic acid at the solution–air interface is not anomalous: the corresponding function ΔE_{HA} assumes positive values, reaching almost 330 mV, which is extremely close to the corresponding values of this function for butyric, valeric, and caproic acids (349, 355, and 340 mV respectively)[69]. The negative values of $\Delta\epsilon$ for a voltaic cell of type (B) are caused by the fact that the liquid junction potential in this cell shifts faster than ΔE_{HA} and in the opposite direction, reaching a value of about 400 mV for concentrated formic acid.

It is striking that, in the range of compositions from 0 to 35 mole % HCOOH, there is a sharp variation of both ΔE_j and the acidity of the medium. For this reason, in a cell of type (B′) the concentration variation of the potential of the hydrogen electrode, due to the changes in the acidity of the medium, is partly compensated by the corresponding variation of ΔE_j. As a result, measurements using cells of type (B′) lead to low pH values, which incorrectly reflect the acidity of the HCOOH–H_2O solutions. Low Hammett acidity functions H_0 have also been observed for such solutions[68], but the reason for this has not been established accurately. They are probably caused by the specific interaction of the indicator base, used for the measurement of H_0, with formic acid, of the type observed by Kolthoff and coworkers[70].

Table 9. The acidity functions pa_H^r and pH, the adsorption potentials of acetic acid, and the changes in the compensating potential and the liquid junction potential in cell (B) for 0.01 M HCl solutions in CH_3COOH–H_2O mixtures at 25°C.

CH_3COOH, mole %	pa_H^r		pH	$\Delta\varepsilon$, mV	ΔE_{HA}, mV	ΔE_j, mV
	pure solns.	solns. with added oenanthic acid				
0	2.10	2.10	2.10	—	—	—
1	4.00	1.95	2.04	127	121	5
2	4.66	1.80	1.97	179	169	10
4	5.23	1.50	1.86	242	221	21
6	5.57	1.20	1.76	292	259	33
8	5.81	0.95	1.68	331	288	43
10	5.93	0.80	1.60	351	304	47
12	5.94	0.75	1.50	351	307	44
15	5.91	0.70	1.40	350	308	42
20	5.89	0.60	1.22	350	313	37
30	5.73	0.40	0.86	342	315	27
40	5.42	0.15	0.46	330	312	18
50	5.05	−0.15	0.02	318	308	10
60	4.66	−0.55	−0.50	311	308	3
70	4.18	−1.20	−1.15	315	318	−3
80	3.58	−1.90	−2.00	318	324	−6
90	2.84	−2.50	−2.85	295	316	−21
100*	2.00	−3.25	−3.80	282	315	−33

*Found by extrapolation.

The stabilisation of the χ-potentials of 0.01 M HCl solutions in acetic acid–water mixtures has been studied[71]. The results are compiled in Table 9. The values for 100% acetic acid were obtained by extrapolation. The surface-active agent (caproic acid) stabilises the surface potentials of the solutions (at least at low acetic acid concentrations), as shown by the markedly different values of pa_H^r for the pure solutions and the solutions stabilised by caproic acid. The function ΔE_{HA} for acetic acid assumes positive values, reaching approximately 320 mV, which is a little less than the corresponding values for formic[66,67], butyric, valeric, and caproic acids[69].

As for HCOOH–H_2O mixtures, a fairly sharp variation of the acidity of the medium and of the liquid junction potential in a cell of type (B) at low acetic acid concentrations (up to 10 mole %) is characteristic of CH_3COOH–H_2O mixtures and these two effects again partly cancel out, as a result of which the pH of these solutions, determined with the aid of cells of type (B′), varies more slowly with solvent composition than pa_H^r. According to Schwarzenbach and Stensby[72], H_0 varies even more slowly. At high acetic acid concentrations, pH overtakes pa_H^r. This may be associated with the unusual dependence of the liquid junction potential on solvent composition, the potential shifting towards negative values at low acetic acid concentrations, reaching a minimum of 10–15 mole% of acetic acid and then slowly shifting towards positive values at high concentrations. This behaviour of ΔE_j appears strange and may be associated with an experimental error. This is suggested also by the finding that the ΔE_{HA} function for acetic acid does not reach values characteristic of caproic and other carboxylic acids and the ΔE_{HA}–composition curve for the CH_3COOH–H_2O mixtures passes through a maximum. At high acetic acid concentration the introduction of caproic acid into the solutions probably does not adequately stabilise the surface potential. The problem of the stabilisation of the χ-potential in the CH_3COOH–H_2O system requires further study.

Table 10. The compensating and liquid junction potentials in cell (B), the adsorption potentials of CH_3OH, and the $\lg \gamma^{\circ r}_{H^+}$ for hydrogen ions in dilute HCl solutions in CH_3OH–H_2O mixtures at 25°C.

CH_3OH, mole %	$\Delta\varepsilon$, mV	ΔE_j, mV	ΔE_{CH_3OH}, mV	$\lg \gamma^{\circ r}_{H^+}$	CH_3OH, mole %	$\Delta\varepsilon$, mV	ΔE_j, mV	ΔE_{CH_3OH}, mV	$\lg \gamma^{\circ r}_{H^+}$
2	107	7	100	0.12	40	344	58	286	1.12
4	168	13	155	0.20	50	353	66	288	1.25
6	201	17	184	0.29	60	360	73	287	1.31
8	230	21	209	0.36	70	365	79	286	1.27
10	248	24	224	0.41	80	369	84	285	1.02
20	301	39	262	0.70	90	372	89	283	0.72
30	328	50	278	0.93	100	375	93	282	0.77

The assumed constancy of the surface potential has been used to determine the medium effects of H^+ ions on passing from water to methanol[73]; the surface potentials of dilute HCl solutions in aqueous alcoholic solvents were stabilised by heptyl alcohol. The results are illustrated in Table 10. As regards certain features, they resemble the results for HCOOH–H_2O and CH_3COOH–H_2O mixtures. In particular, at low methanol concentrations in the solvent both the acidity of the medium (pa_H^r) and the liquid junction potential vary sharply. Therefore, in a cell of type (B′) the shift of the hydrogen electrode potential due to the change in the acidity of the medium is overlapped by the corresponding more marked shift of ΔE_j, as a result of which the pH values measured with the aid of this cell yield incorrect information about the acidity of the aqueous alcoholic HCl solutions. In contrast to the

behaviour of the HCOOH–H_2O and CH_3COOH–H_2O mixtures, small amounts of added organic solvent do not increase but actually decrease the acidity of the medium and the liquid junction potential shifts towards positive values rather than to negative values.

The above features and also the results discussed previously for the HCl–H_2O, $HClO_4$–H_2O, HBr–H_3O, NH_3–H_2O, and N_2H_4–H_2O systems suggest that there is at least a qualitative correlation between the variation of the acidity of the medium and the corresponding variation of the liquid junction potential: an increase of acidity is accompanied by a shift of the liquid junction potential towards negative values, while a decrease of acidity corresponds to a positive shift of ΔE_j. In other words, with decreased basicity of the medium, the tendency of H^+ ions to cross the test solution–saturated KCl solution interface is weaker than for ions of the opposite sign. However, a quantitative correlation cannot be observed. It is appropriate to mention here that the idea of a relation between the acid–base interactions in solutions and the anomalous mechanism of charge transfer by H^+ ions has already been suggested in the literature [74]. Continuing the analysis of the results of experiments on the stabilisation of the χ-potentials of aqueous alcoholic HCl solutions, mention must be made of the fact that there is a qualitative agreement between the results obtained from the analysis of the dependence of the functions $\lg \gamma^{\circ r}_{H^+}$, $\lg \gamma^{\hat{r}}_{H^+}$, and H_0 on the composition of the aqueous alcoholic solvent [8,55]. The sharp decrease of the acidity of the medium following the addition of small amounts of methanol to water is consistent with the changes in the other volume properties of electrolytes in alcohol–water mixtures and with the changes in the volume properties of the mixtures themselves, which can be explained by the stabilisation of the water structure in the presence of alcohol molecules [75,76].

It is known that the addition of inorganic salts to water usually leads to an increase in the surface tension of the solutions formed, as a result of which the surface layers of such solutions are depleted in the electrolyte. According to the calculations of a number of investigators [77,78], the thickness of the surface layer free from the electrolyte ranges from 3 to 5 Å for dilute aqueous solutions of strong electrolytes. This suggests that the surface potentials of electrolyte solutions, whose ions exhibit a weak tendency towards specific adsorption at the solution–air interface, do not differ significantly from the surface potential of pure water. This is valid also for fairly dilute solutions of weak electrolyte, which are not very active at the solution–air interface. If this is true, the voltaic cells of type (A) or (A′) can be used to compare the activities of individual ions (in particular the medium acidities) in such solutions or to estimate ΔE_j without introducing into the test solutions surface-active agents in order to stabilise the surface potential. Direct evidence for the weak influence of electrolytes on the surface potentials of solutions has been published [79–81]. The acidities of standard buffer solutions have been compared without the stabilisation of the potentials [82] and it has been shown that the values of pa^r_H obtained using a voltaic cell of type (A) do not differ from the corresponding values of pa_H (to within 0.02). A standard hydrogen phthalate buffer solution was an exception for reasons which are not altogether clear; according to the results of Kamienski et al [83] both potassium hydrogen phthalate and phthalic acid are surface-active.

The acidities of dilute HCl solution and standard buffer solutions have been compared in the presence of high concentrations of neutral salts [84,85]. The main result of these studies is that the values of pa^r_H and pH agree over fairly wide ranges of the concentrations of the supporting salt. Thus pH and pa^r_H for 0.01 M HCl solution agree up to LiCl, NaCl, and KCl concentrations of 3.5, 3.0, and 1.5 M respectively. The discrepancies between pH and pa^r_H at higher concentrations of the neutral salts can be naturally accounted for by a shift of the χ-potential of the solution due to the appearance of electrolyte ions in the surface layer. Then anions, which are less hydrated, are on average distributed closer to the solution–air interface than cations. A definite inference can be drawn about the diffusion potential at the interfaces between concentrated salt solutions and the saturated KCl solution. The agreement between pH and pa^r_H over a fairly wide range of concentrations of the neutral salts suggests that the diffusion potential varies little with salt concentration and the measurements of the pH of salt solutions in cells with transport are fairly reliable. One should not expect an appreciable effect of acidity on ΔE_j in concentrated salt solutions, of the kind observed in the systems discussed above, since charge transfer across the liquid junction is effected by the salt ions and not H^+ ions.

In conclusion the following remarks may be made. The technique involving the stabilisation of the surface potentials of solutions makes it possible to obtain information about the thermodynamic characteristics of individual ions and liquid junction potentials, which are in good agreement with data found by other non-thermodynamic methods. In many cases this makes it possible to obtain completely new data (for example, for the HCOOH–H_2O, CH_3COOH–H_2O, NH_3–H_2O, and N_2H_4–H_2O systems), which had been hitherto outside the scope of other methods. The technique involving the stabilisation of the χ-potentials of solutions yields fairly accurate values of the adsorption potentials of a number of substances (for example, HCl, HBr, $HClO_4$, HCOOH, CH_3COOH, CH_3OH, NH_3, and N_2H_4) at the solution–air interface, which until now could not be achieved owing to the miscibility of these substances with water and owing to the influence of the liquid junction potentials. The knowledge of the adsorption potentials makes it possible to set up a scale of χ-potentials for a number of solvents and media (adopting as the zero point for the readings the χ-potential of water, the absolute value of which is not yet known reliably): CH_3OH (280–290 mV); HCOOH (320–330 mV); CH_3COOH (320–350 mV); 20 mole % HCl–H_2O (about −350 mV); 25 mole % HBr–H_2O (about −210 mV); 10 mole % $HClO_4$–H_2O (about −115 mV); 10 mole % NH_3–H_2O (about 290 mV); 18 mole % N_2H_4–H_2O (about 330 mV). The χ-potential scale may prove useful in the derivation of information about the chemical potentials of individual ions on the basis of the experimental values of the real potentials of these ions.

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The Oxygen Dimers, Clusters, and Cluster Ions in the Gas Phase

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The formation, thermodynamic properties, and chemical reactions of neutral and charged oxygen clusters of the type O_{2n} ($n \geqslant 2$), (O_4^- and $O_4^+ - O_{18}^+$) as well as oxygen clusters with other molecules (N_2, N_2O, SO_2, H_2O, CO_2, NO, and CO) are examined.
The bibliography includes 49 references.

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I. INTRODUCTION

In a mass-spectrometric study of oxygen which had passed through an ozoniser Grundland[1] observed in 1953 weak currents due to ions with masses of 48 and 64 and attributed them to the presence in the ozonised oxygen of ozone (O_3) and "oxozone" (O_4) molecules. He was apparently the first to attempt the detection in oxygen at normal temperatures and pressures of polymeric oxygen molecules as well as oxygen ions with large masses.

Although Grundland's data were subsequently disproved in a number of studies[2-4], the presence of dimeric molecules O_2-O_2 in oxygen under normal conditions and the formation of clusters on adiabatic expansion of the gas has been recently demonstrated mass-spectrometrically and spectroscopically.

Improvements in technique of mass-spectrometric and certain other physical research methods for reactions in gases made it possible to investigate the thermodynamics and kinetics of the formation of positive and negative oxygen cluster ions $O_{2n}^{\pm}$ and also heteromolecular oxygen cluster ions $O_{2n}^{\pm}X_kY_lZ_m$ incorporating neutral molecules X, Y, and Z such as H_2O, CO_2, and NO.

It has been shown mass-spectrometrically[5,6] that these ions are very reactive. One of the causes of this is their capacity to form a relatively long-lived ion-molecule (molecules) complex, i.e. a cluster ion. The reaction time proved to be sufficient for bond rearrangement[7]. For example, the complex $O_2^-.H_2O$, formed as an intermediate in the reduction of oxygen by low-energy electrons, plays an important role in the chemistry of the ionosphere. Other oxygen cluster ions are also characteristic of the chemistry of the low-temperature plasma and of the radiation chemistry of gases.

The bond in the $AB^{\pm}$ cluster ion is mainly due to the polarisation of the molecule A under the influence of the ion $B^{\pm}$; the bond energy is given to a first approximation by the equation $V_n = -\alpha e^2/2r^4$, where α is the polarisability of the molecule A, r the distance between the centres of A and $B^{\pm}$, and e the electronic charge.

Comparison with experimental values of bond energies and other parameters of oxygen cluster ions, which have now been calculated by quantum-mechanical and statistical physical methods, yields valuable data for the theory of the chemical bond. The knowledge of the chemistry of oxygen cluster ions may be useful in the development of ways of synthesising new potential sources of oxygen which are valuable in practice.

II. THE O_4 MOLECULE, OXYGEN CLUSTERS

The existence of O_4 molecules is due to weak intermolecular interactions. The bond strength in such molecules is hundreds of times smaller than in the usual chemical compounds, for example the O_2-O_2 bond energy has been estimated as 460 cal $mole^{-1}$.[8]

The interaction of oxygen molecules in the gas phase leads to three types of binary species: collision pairs, metastable dimers, and bound dimers[9]. The collision pair is a pair of molecules in the gas phase subjected to appreciable mutual attraction (the molecules are usually separated by a distance of 5-10 Å during the collision) and having a kinetic energy greater than the height of the potential barrier on the intermolecular potential. The lifetime of the molecules of this type has been estimated as 10^{-13} s under the usual conditions.

When a so-called "triple" collision occurs and the third species acquires part of the kinetic energy of the other two colliding molecules, the metastable dimer—the O_2-O_2 molecule with energy greater than its dissociation energy but smaller than the maximum on the potential curve—may be formed. The lifetime of the metastable dimer has been estimated as $10^{-11}-10^{-16}$ s. The triple collision can result also in the formation of the bound dimer—a stable molecule with energy below the dissociation energy of the O_2-O_2 bond.

Metastable dimers can decompose spontaneously as a result of the tunnel effect. Since the rotational energy of the dimer in the gas phase at normal temperatures is comparable to the depth of the well on the potential energy curve for the dimer, the concentrations of the bound and metastable dimers are approximately equal.

The O_2 molecule does not have a dipole moment and therefore does not absorb in the infrared. On contact with another molecule, its quadrupole moment generates a dipole moment in its neighbour, which modulates the vibrational and rotational frequencies of the molecule, so that absorption in the infrared becomes possible. In other words, the pair of colliding oxygen molecules

absorbs due to transitions which are forbidden in the absence of the collision. The bands of such absorption should be broad and diffuse owing to the short lifetime of the colliding pair. On the other hand, the bound dimer should give rise to narrow absorption bands in consequence of its relatively long lifetime.

There are numerous spectroscopic data showing that at room temperature oxygen contains only collision pairs[10,11,12]. The infrared spectra of solutions of oxygen in liquid nitrogen show a broad shoulder on the vibrational absorption band induced by collisions, which vanishes on dilution; this phenomenon can be attributed to the presence of the dimer[13].

However, the infrared absorption spectrum of solid oxygen does not support the conclusion that individual $(O_2)_2$ molecules exist[14]. An X-ray diffraction study of solid oxygen also ruled out the presence of dimeric species[15]. In 1971 Long and Ewing[16] obtained the infrared absorption spectrum of gaseous oxygen (Fig. 1) at 87 K and a pressure of 559 torr for an optical path length of 152 m. A diffuse doublet with the centre at 1591.2 cm^{-1} was observed. The doublet had components with a width $\Delta\nu_{1/2} \simeq 7$ cm^{-1} and with centres at 1586.1 and 1596.6 cm^{-1}. These data confirm the presence of bound dimers in gaseous oxygen, which naturally exist also at other temperatures.

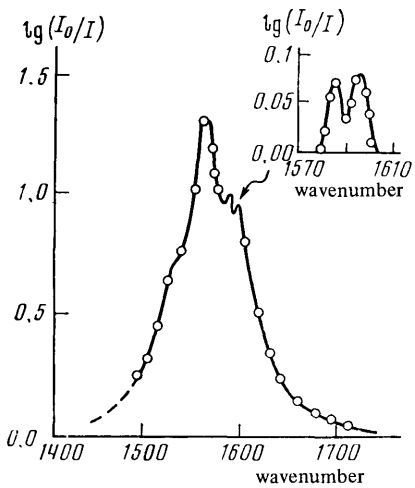

Figure 1. The infrared spectrum of gaseous oxygen induced by collisions.

The energy of formation of $(O_2)_2$ observed in the above study is 830 cal $mole^{-1}$, in good agreement with the value calculated by Stogrin and Hirschfelder[17]. The lifetime of the absorbing species is linked to the width of the corresponding line by the relation $\tau = (2\pi c\Delta\nu_{1/2})^{-1}$. The lifetime of the oxygen dimer, estimated from the doublet width $\Delta\nu \simeq 7$ cm^{-1}, is 10^{-12} s. This shows that the absorbing O_4 species must be regarded as the bound dimer. The actual lifetime of the dimer is somewhat greater than the above value, since the doublet contains a number of unresolved lines.

In 1966 Leckenby and Robbins[18] demonstrated mass-spectrometrically for the first time the presence of dimers in gaseous oxygen at the usual temperature and pressure. The oxygen dimers were detected with the aid of a mass-spectrometer of special design, in which oxygen was admitted into an ion source of the open type through an aperture in a 1 μm foil, the ion accelerating and ion focussing plates having been replaced by grids to increase the pumping rate. The concentration of the $(O_2)_2$ dimers in oxygen at a pressure of 100 torr and 300 K amounted to about 5×10^{-7}.

Previously Leckenby et al.[19] detected mass-spectrometrically dimers, trimers, and heavier clusters in a number of gases, including oxygen, during supersonic adiabatic flow of the gas from a reservoir (of gas pressures up to 40 atm) into a high vacuum maintained by a powerful pump. They found that the variation in the concentration of clusters with the reservoir temperature and pressure is approximately the same for each of the gases investigated; the differences are determined by the critical temperature T_c and pressure p_c and the ratio of the specific heats $C_p/C_V = \gamma$ for the given gas. It was noted that, for gases with similar critical constants T_c and p_c but with different values of γ, the maximum concentration of the polymer is observed at different pressures in the reservoir. Thus in argon ($T_c = -122°C$, $p_c = 48$ atm, $\gamma = 1.66$) the maximum concentration of clusters is reached at a reservoir pressure of 20 atm (at about $\sim 20°C$), while in oxygen ($T_c = -119°C$, $p_c = 50$ atm, $\gamma = 1.40$) it is reached at a pressure in excess of 50 atm. It was also established that gases with high values of γ show a greater tendency towards the formation of clusters.

On the other hand, for gases with similar values of γ the tendency towards polymerisation is determined by the critical constants. Oxygen ($T_c = -119°C$, $p_c = 50$ atm, $\gamma = 1.40$) exhibits a greater tendency towards the formation of clusters than nitrogen ($T_c = -147°C$, $p_c = 33.5$ atm, and $\gamma = 1.40$). In experiments with compressed air the formation of the dimers $(N_2)_2$, N_2O_2, and $(O_2)_2$ in the proportions 1 : 0.3 : 1.6 was observed. The concentration of clusters increases rapidly with increase of gas pressure in the reservoir, reaches a distinct maximum, falls, and then increases again.

Green and Milne[20] also observed the formation of oxygen cluster molecules during the supersonic flow of oxygen under analogous conditions. In 1972 Golomb and Good[21] demonstrated mass-spectrometrically the formation of dimers, trimers, and oligomeric clusters (up to molecules with a mass of 600) in the supersonic adiabatic flow of a number of gases into a vacuum. The maximum concentration of the oxygen dimer was observed at an O_2 pressure in the reservoir-source of 200 torr and a temperature of 400 K.

The clusters thus detected have come to be regarded as condensation "embryos" in the supercooled gas. This view is supported by the finding that gases with high values of T_c, p_c, and γ, i. e. with a considerable tendency towards condensation, show a greater tendency towards the formation of clusters.

Thus the existence of the oxygen dimers (O_2) in the gas under the usual conditions and also of clusters with a high molecular weight in the stream during the supersonic adiabatic flow of the gas must now be regarded as firmly established.

III. OXYGEN CLUSTER IONS

A considerable proportion of studies on the equilibria and rates of formation and decomposition of negative cluster ions were made using instruments consisting of a

combination of a drift tube and a mass-spectrometer[22-25]. A potential difference is applied between two electrodes in a tube 2.5 cm in diameter; these define the drift region (usually 2.5–3 cm long). The primary negative ions are formed by electron impact at the beginning of the drift tube[26]. The electron source is a heated filament or a photocathode. The ions pass from the drift tube to the mass analyser through an aperture of small diameter (25–250 μm) in the centre of the anode. Such devices sometimes operate under pulsed conditions, the ions and electrons being admitted into the drift space in pulses lasting between 1 and 20 μs, which amount to about 1% of the drift time[27,28].

Another type of instrument used in the study of reactions of oxygen cluster ions, in particular positive ions, is the high-pressure mass-spectrometer. Positive ions are obtained by a pulsed electron beam with energies up to 4 keV. The ions drift from the field-free space in the ion source to the inlet aperture in the mass analyser. At pressures up to 10 torr the reaction time reaches some hundreds of microseconds[29]. The use of such a device with pulsed operation for the study of reactions in the absence of a field was first described by Tal'roze and Frankevich[30]. The duration of the electron pulse was usually 10 μs, the time during which the inlet to the mass analyser is open also being 10 μs; the period between the pulses (2 ms) is sufficiently long for the ion current due to the preceding pluse to disappear completely.

The instrument makes it possible to record the time variation of the current due to each ion investigated. In continuous-operation devices the ion–molecule reaction takes place in a field where ions have a kinetic energy exceeding by 1–3 orders of magnitude the thermal energy corresponding to the temperature of the walls of the ionisation chamber. The reaction velocities obtained in such apparatus must be extrapolated to zero field. Such extrapolation involves errors, since the variation of the reaction rate with field strength is not always simple. Pulsed operation devices make it possible to avoid these complications.

A series of studies were made on equilibria involving positive cluster ions of oxygen in low-pressure mass-spectrometers using tritium as the source of ionising radiation[31]. In such apparatus the reaction time is about 1 ms and the time resolution achieved by the amplifier is better than 1 μs.

Reactions involving the formation of heteromolecular oxygen cluster ions and the exchange reactions of the neutral molecule in the cluster were studied using flow apparatus in a stream of carrier gas (helium, argon, etc.). Such flow apparatus makes it possible to investigate the reactions at temperatures from 80 to 600 K and pressures up to 10 torr. Oxygen is ionised by electron impact in the ion source located at the beginning of the tube through which the stream of gas is flowing. The reaction products are detected with a quadrupole mass analyser.

IV. THE O_4^- ION

The early attempts to detect the O_4^- ion in oxygen at 300 K and a pressure in the range 0.6–3 torr using a drift tube[32-34] were unsuccessful, although in analogous experiments at 77.4 and 87.6 K Voshall et al.[35] detected the O_4^- ion and estimated its dissociation energy as 0.06 ± 0.006 eV (1.4 ± 0.2 kcal mole^{-1}) from the temperature variation of the equilibrium constant for the formation and decomposition of O_4^-. On the basis of their results, the authors[35] concluded that the O_4^- ion cannot be detected in the drift tube above 195 K. However, theoretically it was to be expected that the O_4^- ion should be approximately as stable as the O_4^+ ion investigated previously ($\Delta H = -9.6$ kcal mole^{-1}).[36]

Using a high-pressure mass-spectrometer and titanium tritide as a 2 c source of ionising radiation, Conway and Nesbitt[37] detected the O_4^- ion and determined the equilibrium constant for the reaction $O_2^- + O_2 \rightleftharpoons O_4^-$ at temperatures from 273.2 to 352.8 K and oxygen pressures of 6.9 and 12 torr. The equilibrium constants (K, torr^{-1}) for the formation of O_4^- are listed below

T, °K	6 torr	9 torr	12 torr	K_{av}
273.2	9.46 *	10.6 *	10.7	10.3
293.0	1.58	1.55	1.61	1.58
313.4	0.323	0.344	0.335	0.334
333.0	0.102	0.106	0.102	0.103
352.8	0.0323	0.0341	0.0368	0.0344

* Determined for a flow reaction.

ΔH°_{298} for the formation of O_4^-, calculated from the above equilibrium constants, is −13.55 ± 0.16 kcal mole^{-1} (0.59 eV).

Using an improved drift tube, McKnight and Sawina[28] obtained curves relating the relative concentrations of O_4^- and O_2^- ions to drift time in oxygen at 310 K and pressures from 0.5 to 4 torr and found that the equilibrium constant for the formation of O_4^- is 0.5 torr^{-1} (1.6×10^{-17} cm^3), which virtually agrees with the above data of Conway and Nesbitt[37]. McKnight and Sawina[28] measured for the first time the rate of the termolecular reaction involving the formation of O_4^-:

$$O_2^- + 2O_2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} O_4^- + O_2 \ .$$

The rate constant k_1 for this reaction is 3×10^{-31} cm^6 mol.$^{-2}$ s^{-1} at 310 K. The rate constant for the reverse reaction was found from the rate constant for the forward reaction and the equilibrium constant: $k_2 = 2 \times 10^{-14}$ cm^3 mol.$^{-1}$ s^{-1}.

Pack and Phelps[38] studied recently the reactions of negative oxygen ions on apparatus consisting of a combination of a drift tube and a quadrupole mass analyser and found that the rate constants for the forward and reverse reactions in the formation of the O_4^- ion are $k_1 = 4 \times 10^{-31}$ cm^6 mol.$^{-2}$ s^{-1} and $k_2 = 2.7 \times 10^{-14}$ cm^3 mol.$^{-1}$ s^{-1} respectively, which agrees well with McKnight and Sawina's data[28]. Thus the reaction of O_2^- with O_2 is fairly rapid, the system reaching equilibrium with a time constant of 1 ms at an oxygen pressure of 1 torr.

The detection of O_4^- ions with the aid of the mass-spectrometer is difficult, since their content at equilibrium is smaller by a factor of 2 than that of O_2^- ions at 310 K and 1 torr and the time constant for equilibration increases with decrease of pressure. In the presence of traces of CO_2 the O_4^- ion is converted into CO_4^- as a result of the reaction $O_4^- + CO_2 \xrightarrow{k} CO_4^- + O_2$ ($k = 4.3 \times 10^{-10}$ cm^3 mol.$^{-1}$ s^{-1}), which masks still further the O_4^- ion (at a CO_2 partial pressure of 10^{-5} torr the time constant for this reaction is 10 ms).[39]

Lecuiller et al.[40] detected the O_4^- ion in the zone of the corona discharge between the surface of an aqueous $FeSO_4$ solution and a negatively charged knife edge (2–30 kV) together with the negative oxygen ions O^-, O_2^-, and O_3^-; they found that the relative concentrations of O_3^- and O_4^- ions depend greatly on the discharge current (0–70 μA). O_4^- ions should be present in the atmosphere, since at a height of 40 km they are formed as a result of the reaction between O_2^- and O_2 with a time constant less than 10 ms;

the presence of CO_2 and H_2O in the troposphere promotes the conversion of O_4^- into water and carbon dioxide clusters followed by their reactions[28].

It is of interest to compare the rates of formation of O_4^- and O_4^+. Durden et al.[29] found that the rate constant for the formation of O_4^+ is 2.8×10^{-30} cm^6 s^{-1} at 298 K and also determined the dissociation energy of the O_4^+ ion as 0.4 eV, while, as stated above, the dissociation energy of the O_4^- ions is 0.58 eV.[37] Thus the rate of formation of the negative cluster ion is smaller by an order of magnitude than the rate of formation of the positive ion, although the bond energy in the negative ion is greater than in the positive ion. Apparently it does not necessarily follow that the higher the bond energy the higher the rate of formation of the cluster ion. The properties of the O_4^- ion investigated show that the ion plays a major role in systems involving negative oxygen ions, for example in the reactions of electrons in the lower layers of the atmosphere.

V. THE O_4^+–O_{18}^+ OXYGEN CLUSTER IONS

In 1964 Yang and Conway[36] determined the equilibrium constant for the reaction $O_2^+ + 2O_2 \rightleftharpoons O_4^+ + O_2$ at temperatures from 239 K to 344 K and oxygen pressures from 1 to 9 torr with the aid of a high-pressure mass-spectrometer and titanium tritide as a 400 mc source of ionising radiation in oxygen. These data are presented in Table 1.

Table 1. The equilibrium constants (K, torr^{-1}) for the reaction $O_2^+ + O_2 \rightleftharpoons O_4^+$.

T, °K	p_{O_2}, torr	K, torr^{-1}	T, °K	p_{O_2}, torr	K, torr^{-1}
259	1.00	3.8	320	1.00	0.097
259	2.00	4.8	320	2.00	0.094
259	9.00	5.7	320	4.00	0.106
			320	9.00	0.121
273	1.00	1.30			
273	2.00	1.49	344	1.00	0.036
273	4.00	1.61	344	2.00	0.035
273	9.00	1.76	344	4.00	0.037
			344	9.00	0.045
293	1.00	0.41	—	—	—
293	4.00	0.56	—	—	—
293	9.00	0.81	—	—	—

The familiar relation

$$\Delta F_{T_2} - \langle \Delta C_p \rangle_{av} \left(\Delta T - T_2 \ln \frac{T_2}{T_1} \right) = \Delta F^\circ_{T_1} - \Delta S^\circ_{T_1} \Delta T, \qquad (1)$$

where $\Delta F^\circ_{T_1}$ is the Gibbs free energy of reaction under standard conditions linked to the equilibrium constant K (Table 1) by the relation $\Delta F^\circ_{T_1} = -RT_1 \ln 760 \times K$ and $\langle Cp \rangle_{av} = 2.8$ cal mole^{-1} deg^{-1} is the average change in heat capacity in the above temperature range, was used to determine the thermodynamic characteristics of the reaction. The estimate was based on the assumption that O_4^+ is a rigid linear complex with a distance of 3.0 Å between the centres of O_2 and O_2^+; it was also assumed that the distance between the centres of the atoms in O_2^+ is equal to the corresponding distance in O_2; $\Delta S^\circ_{T_1}$ is the standard entropy of reaction at a temperature T_1. Graphical solution of Eqn. (1) gave $\Delta S^\circ_{293} = -20$ e.u. and $\Delta F^\circ_{293} = -3.56$ kcal mole^{-1}. Hence $\Delta H^\circ_{293} = -9.60$ kcal mole^{-1} (0.416 eV).

In 1965 Conway and Yang[41] estimated mass-spectrometrically the equilibrium constants for the formation of positive homomolecular oxygen cluster ions ($O_{2n}^+ + O_2 = O_{2n+2}^+$ with $n = 2$–5) at a low temperature (Fig. 2).

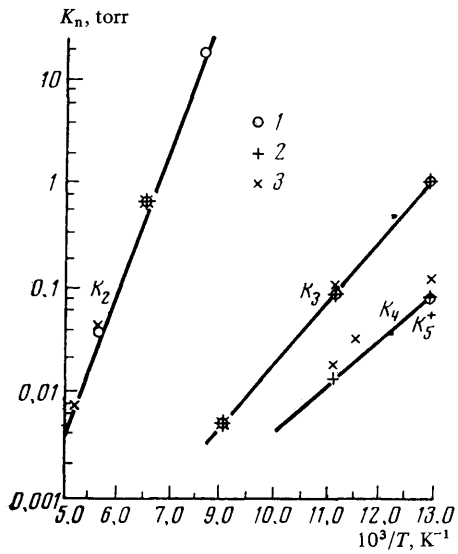

Figure 2. Temperature variation of the equilibrium constants K_n of reactions of the type $O_{2n}^+ + O_2 = O_{2n+2}^+$; oxygen pressure (torr): 1) 1; 2) 2; 3) 4.

In 1970 Conway and Janik[42] repeated the previous study and refined the results for the O_4^+–O_{18}^+ cluster ions, using a somewhat improved research technique. Table 2 lists the observed equilibrium constants for the formation of the cluster ions by the reaction $O_2 + O_{2n}^+ \rightleftharpoons O_{2n+2}^+$.

Table 2. The equilibrium constants K_n for the reactions $O_{2n}^+ + O_2 \rightleftharpoons O_{2n+2}^+$.

n	T, °K	p_{O_2}, torr				Multiplier
		1,55	3,09	6,15	9,14	
3	77.3	1.07	1.10	1.18	1.26	·100
3	90.1	1.03	1.02	1.06	1.16	·10^{-1}
4	77.3	8.02	8.21	9.37	10.78	·10^{-2}
4	90.1	—	0.79	1.03	1.31	·10^{-2}
5	77.3	4.50	4.47	5.21	5.95	·10^{-2}
5	90.1	—	—	8.48	9.30	·10^{-3}
6	77.3	—	—	2.77	3.30	·10^{-2}
7	77.3	—	—	1.90	2.40	·10^{-2}
8	77.3	—	—	—	1.70	·10^{-2}

The standard enthalpies and entropies of formation of the cluster ions by the reaction $O_2 + O_{2n}^+ = O_{2n+2}^+$ and the corresponding bond energies were calculated from the observed low-temperature equilibrium constants (77–90 K) and the models adopted for the ions (Table 3).

Conway[43] calculated the energies of the O_4^+ and O_4^- ions (together with N_4^+) by a somewhat modified MO-SCF method for structures with C_2 symmetry as a function of the angles $\theta = \theta'$ and the distance R between the interacting species (Fig. 3). The equilibrium dissociation energies D_3 for the equilibrium distances R_e and angles θ_e are listed below:

Ion	D_e, kcal mole^{-1}	R_e, Å	θ_e, deg	D(expt.), kcal mole^{-1}
O_4^+	11.66	2.03	—67	10,8
O_4^-	8.49	2.08	—71	13,6
N_4^+	34.7	2.04	0	11,5

Table 3. Thermodynamic characteristics of the reactions $O_2 + O_{2n}^+ = O_{2n+2}^+$.

n	ΔS, e.u.	ΔH°, kcal mole^{-1}	$D_0(O_2-O_2^+)$	$D_e(O_2-O_2^+)$*
1	—25.01±0.2	—10.84±0.05	10.53±0.10	11.58±0.11
2	—31.78±0.3	—6.87±0.06	6.51±0.07	7.72±0.13
3	—19.8(—0.3+1.0)	—2.54(—0.03+1.0)	2.56(+0.16—0.06)	2.88(+0.07—0.71)
4	—23.9(—0.5+2.1)	—2.46(—0.05+0.18)	2.43(±0.06—0.09)	2.81(+0.01—0.30)
5	—17.0(—3.0+9.2)	—1.84(—0.3+0.7)	2.00(±0.4—0.6)	2.13(+0.4—1.0)

* $D_e(O_2 - O_2^+)$ is the dissociation energy corresponding to the minimum in the potential energy curve.

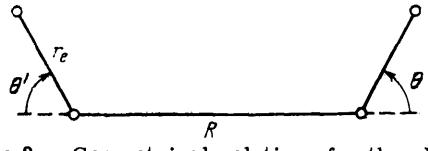

Figure 3. Geometrical relations for the planar ion–molecule complex.

Durden et al.[29] also determined the rate constants for the formation of the O_4^+ ion and its dissociation energy using a high-pressure mass-spectrometer with a pulsed electron beam having an energy of 4 keV as the source of ionising radiation. They succeeded in following the decrease of the concentration of O_2^+ ions and the increase of the concentration of O_4^+ ions in oxygen after the electron pulse (at an oxygen pressure of 3–4 torr) before the equilibrium concentrations of these ions were reached. Equilibrium was attained 60 μs after the pulse at 298 K and after 20–30 μs at 341 K. The rates of formation of O_4^+ were also determined in other investigations[29,44,46,47] and in a study by Joung and Falconer[45]. Using the mass-spectrometric method for the study of reactions in a stream of carrier gas (helium), Adams et al.[46] investigated at 200 K and an overall pressure of 1.767 torr the equilibrium in the following reaction involving a cluster ion:

$$O_2^+ + O_2 + He \rightleftarrows O_4^+ + He \ .$$

The rate constants for the formation and decomposition of the O_4^+ ion are listed in Table 4.

It is interesting to note that the rate constant for the formation of the cluster ion O_4^+, equal to 2.8×10^{-30} cm^6 mol.$^{-2}$ s^{-1}, is almost a factor of 30 smaller than the rate constant for the corresponding reaction of nitrogen[29] ($N_2^+ + 2N_2 \rightarrow N_4^+ + N_2$), which is 8.57×10^{-29} cm^6 mol.$^{-2}$ s^{-1}.

Table 4. The rate constants for the formation (k_1) and decomposition (k_2) of the O_4^+ ion.

Reaction	°K	k_1, cm^6 mol.$^{-2}$ s^{-1}	k_2, cm^3 mol.$^{-1}$ s^{-1}	Refs.
$O_2^+ + 2O_2 \underset{k_2}{\overset{k_1}{\rightleftarrows}} O_4^+ + O_2$	298	$2.8 \cdot 10^{-30}$	$2.8 \cdot 10^{-13}$	29
»	298	$2.4 \cdot 10^{-30}$	—	44
»	298	$1.5 \cdot 10^{-30}$	—	45
$O_2^+ + O_2 + He \underset{k_2}{\overset{k_1}{\rightleftarrows}} O_4^+ + He$	200	$2.45 \cdot 10^{-30}$	$3 \cdot 10^{-17}$	46,47
	200	$2 \cdot 10^{-31}$	$1 \cdot 10^{-14}$	48

VI. REACTIONS OF HETEROMOLECULAR OXYGEN CLUSTER IONS

Adams et al.[46] measured the rate constants for trimolecular reactions involving the association of O_2^+ with H_2, N_2, O_2, CO_2, NO_2, and SO_2 in a stream of helium as the carrier gas and the third body at temperatures below 300 K, which proceed via the general mechanism

$$A^\pm + B + M \rightarrow A^\pm B + M \ .$$

The rates of association of O_2 with N_2, O_2, and CO_2 at 200 K were also measured.

Since the bond energy and the rate constant for the termolecular reaction vary in the same sense (in agreement with theoretical concepts), the authors[46] found that the molecules can be arranged in the following sequence in order of increasing energy of the bond with the O_2^+ ion: $H_2 < N_2 < O_2 < N_2O < SO_2 < H_2O$. For O_2^-, the stability of the ionic clusters increases in the sequence $N_2 < O_2 < H_2O < CO_2 < NO$. The rates of formation of cluster ions such as $O_2^+.N_2.N_2$, $O_2^+.O_2.N_2$, etc. were also estimated.

Reactions of another type involving the formation of heteromolecular ionic clusters in a stream which have been investigated are the bimolecular exchange reactions of the neutral molecule in the cluster:

$$A^\pm \cdot B + C \rightarrow A^\pm \cdot C + B \ ,$$

where A = O_4^-, O_2^+, O_2^-, or O^- and B and C = O_2, N_2, N_2O, SO_2, H_2O, CO_2, NO, or CO. The rate constants for these reactions were measured at 80, 200, and 300 K. In certain cases the exchange reactions of the neutral molecule in the cluster ion are only weakly exothermic, so that the reverse reaction takes place; it is then possible to estimate the free energies of these reactions (from the equilibrium constants). Since the entropy changes in these reactions should be small, their free energies $\Delta F^\circ = -RT \ln K$ are close to the enthalpies of reaction ΔH. The latter values are approximately equal to the differences between the bond energies of the initial molecules and the resulting cluster ion. This has been confirmed to some extent by data for the equilibrium in the reaction $O_2^- \cdot O_2 + CO_2 \rightleftharpoons O_2^- \cdot CO_2 + O_2$.

It was found that the free energy of this reaction, and hence the approximate difference ΔD between the association energies of $O_2^-.CO_2$ and $O_2^-.O_2$, is 0.26 eV. Pack and Phelps[49] found that the energy of the dissociation of the $O_2^-.CO_2$ ion into O_2^- and CO_2 is 0.8 ± 0.08 eV. On the basis of this value and the value of 0.59 eV obtained by Conway and Nesbitt[37] for the $O_2^- - O_2$ bond energy, we find ΔD = 0.21 eV. Within the limits of experimental error, this agrees with the above value of 0.26 eV.

The data presented for the chemistry of oxygen cluster ions show that much experimental information has already been accumulated in this field and that theoretical studies are being made in order to refine the ideas concerning the nature of the interaction forces in these ions; the results of the two lines of research supplement one another. Evidently in the future research in this field will develop vigorously in connection with the growing interest in the chemistry of the ionosphere, the radiation chemistry of gases, etc.

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The Structures and Reactivities of *Closo*- and *Nido*-carboranes

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The structures, methods of synthesis, and chemical properties of *closo*- and *nido*-carboranes are discussed and certain general features of the chemical reactions of carboranes are indicated.
The bibliography includes 228 references.

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I. INTRODUCTION

Among organic derivatives of the elements, the class of organoboron compounds (carboranes)—compounds having the structure of regular polyhedra or their fragments [1] and consisting of boron and carbon atoms or the atoms of other elements†—shows very great promise.

The most complete compilation of data on the chemistry of carboranes has been published in Grimes' monograph [2] (up to 1970) and in Williams' review [3] (up to 1968). Lipscomb's monograph [4] deals with problems of the theory of the structures and chemical bonding in boron hydrides and carboranes. The latest advances in the chemistry of carboranes have been described systematically in annual reviews [5-8]. Furthermore, individual stages in the development of this field of chemistry were dealt with in a number of early reviews [9-15]. Certain special problems of the chemistry of carboranes are considered in other publications [16-25].

Bearing in mind the considerable interest shown by many investigators in modern problems of the chemistry of organic derivatives of the elements, in particular in the chemistry of carboranes, which is developing vigorously, we thought it useful to supplement and to attempt to survey the available literature data. The main aim of the present review is a consideration of the general characteristics of the chemical reactions of *closo*-, *nido*-, and *arachno*-carboranes, the methods of synthesis, structures, and chemical properties of each representative of these classes of compounds being quoted for reference and illustration.

According to Williams [3], the first information about the existence of carboranes was obtained by Landesman in 1953, who detected by mass-spectrometry ions derived from compounds having the compositions $C_2B_3H_x$, $C_2B_4H_y$, and $C_2B_5H_z$ amongst the pyrolysis products of a mixture of diborane and acetylene, their overall yield with respect to the amount of diborane which reacted being less than 1%. Later, Keilin obtained the same mixture (in a yield of about 2%) from pentaborane(9) and acetylene in an electric discharge. The lower limit to the number of hydrogen atoms, $C_2B_4H_{y\geq 6}$ and $C_2B_5H_{z\geq 7}$, was established on the basis of mass-spectrometric data and it was concluded that the compounds have a closed structure. In 1956 Good repeated this investigation and isolated compounds having the compositions $C_2B_3H_5$, $C_2B_4H_6$, and $C_2B_5H_7$. According to mass-spectrometric, ^{11}B NMR, and ^1H NMR data, the only possible structure for $C_2B_5H_5$ proved to be that of a trigonal bipyramid. Octahedral and pentagonal bipyramidal structures were proposed respectively for $C_2B_4H_6$ and $C_2B_5H_7$. These data were published at the beginning of the 1960s. [26,27] Good and Williams suggested that the compounds obtained be called carboranes. Subsequently, this name was extended also to other compounds whose molecules consist of closed polyhedra or their fragments and contain boron and carbon atoms.

Reports of the synthesis of yet another representative of the family of carboranes—$C_2B_{10}H_{12}$ and its *C*-derivatives obtained from decaborane(14) ($B_{10}H_{14}$) or its complexes with Lewis bases ($B_{10}H_{12}L_2$) and compounds of the acetylene series—were published in 1962-1963. Thermal isomerisation (450-500°C) of the 1,2-isomer yielded the 1,7-isomer [28] and at a higher temperature also the 1,12-isomer of carborane(12). [29]

Carboranes with 9,8,7, and 6 boron atoms in the polyhedron were obtained by the degradation of 1,2- and 1,7-$C_2B_{10}H_{12}$. [30-32] The compound $Me_2C_2B_6H_6$ was isolated by Williams and Gerhart from the products of the reaction of hexaborane(10) with dimethylacetylene [33]. Thus systematic studies yielded all the representatives of the homologous series of *closo*-carboranes having the general formula $C_2B_nH_{n+2}$. *closo*-Carboranes containing one and three carbon atoms in the molecule have now been also synthesised.

Reports of the synthesis of a representative of *nido*-carboranes ($C_2B_4H_8$), i.e. carboranes with an open structure, appeared at the beginning of the 1960s. [34] *nido*-Carboranes containing up to four carbon atoms in the molecule are now known.

$C_2B_7H_{13}$, the first representative of *arachno*-carboranes, was reported in 1966. [35] The second *arachno*-carborane ($C_2B_8H_{14}$) became known comparatively recently [36].

† Compounds containing in the molecule nitrogen, phosphorus, arsenic, sulphur, germanium, silicon, etc. atoms as well as transition metal atoms have been obtained. In the present review the chemistry of heteroboranes, heterocarboranes, metalloboranes, and metallocarboranes is not considered, but the general features of the chemistry of carboranes can be extended also to these classes of compounds.

II. CLASSIFICATION AND NOMENCLATURE. THE NATURE OF BONDING IN CARBORANES

In accordance with Williams' suggestion [1], carboranes are classified as follows: *closo*-carboranes $C_0-_2B_nH_{n+2}$, *nido*-carboranes $C_0-_4B_nH_{n+4}$, and *arachno*-carboranes $C_0-_6B_nH_{n+6}$; the case with C_0 corresponds to boron hydride (boranes).

1. Nomenclature

According to the recommendations by the Commission on Nomenclature of the American Chemical Society [37], the names of these compounds are devised in accordance with the following rules: initially the location of the carbon atoms in the molecule is indicated, then the number of carbon atoms is stated, and a prefix is added characterising the type of structure (*closo*- or *nido*-); next follows a Greek numeral corresponding to the total number of atoms in the molecule and the ending borane is added; finally the number of hydrogen atoms is indicated in brackets.

For anions, the method of forming the name is on the whole the same, but the number of hydrogen atoms is stated at the beginning, the ending borane is replaced by borate, and the charge of the anion is indicated in brackets. For example, the compound 1,10-$C_2B_8H_{10}$ is called 1,10-dicarba-*closo*-decaborane(10), 7,8-$C_2B_9H_{13}$ is 7,8-dicarba-*nido*-undecaborane(13), and 7,8-$C_2B_9H_{12}^-$ is dodecahydro-7,8-dicarba-*nido*-undecaborate(1-).

The fundamental principles of the numbering of atoms in boron hydride and carborane molecules are as follows. In *closo*-carboranes atoms located in planes perpendicular to the highest-order symmetry axis are numbered clockwise in succession starting with the topmost atom. For *nido*-carboranes, one employs their planar projection and the structure is considered from the side opposite to that of the open face. The numbering is also clockwise and begins with the atoms closest to the centre of the projection. The numbering must be such that carbon atoms and those of other elements have the minimum numbers (Fig. 1)

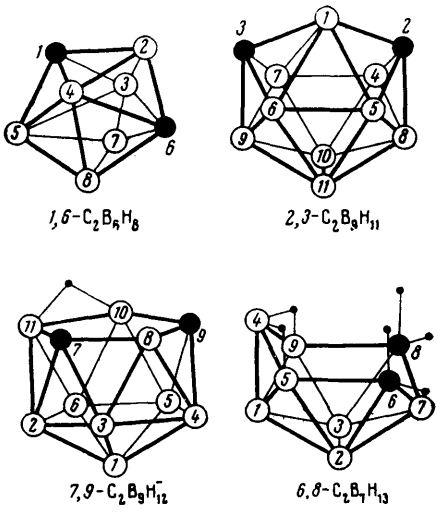


Figure 1.

2. Isoelectronic Series

In the chemistry of carboranes it is convenient to distinguish isoelectronic series [3], i.e. series of compounds whose molecules have the same geometrical and electronic structures, differing from one another in the CH/BH^- or CH/BH_2 ratios of the numbers of different units, BH^- or BH_2 being equivalent to the CH structural unit. As an example, one may quote the series B_6H_{10}, CB_5H_9, $C_2B_4H_8$, $C_3B_3H_7$, $C_4B_2H_6$ or B_6H_8‡, CB_5H_7, and $C_2B_4H_6$ (Figs. 2 and 3).

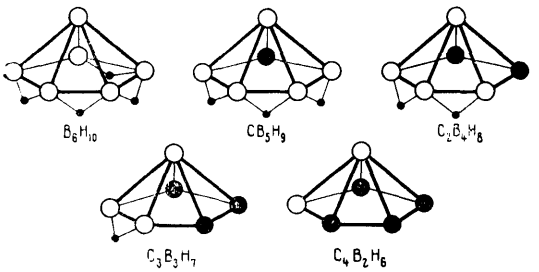


Figure 2.

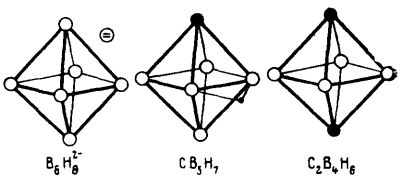


Figure 3.

For *closo*-compounds, the CH/BH^- series can be represented as follows in a general form: $B_{n+2}H_{n+2}^{2-}$, $CB_{n+1}H_{n+2}^-$, and $C_2B_nH_{n+2}$. If this electronic series is extended by yet another CH unit, we obtain the family $C_3B_{n-1}H_{n+2}^+$. A compound of this type must have a positive charge (+1), but the abstraction of a proton should make the molecule neutral as a whole ($C_3B_{n-1}H_{n+1}$). A compound of this type has been obtained ($C_3B_5H_7$); [39] it belongs to the isoelectronic series $C_3B_5H_8^+$, $C_2B_6H_8$, ($CB_7H_8^-$), and $B_8H_8^{2-}$ (Fig. 4).

The following series may be quoted as an example of a CH/BH^- isoelectronic series of compounds with an open structure: $C_2B_8H_{12}$§, CB_9H_{12}¶, and $B_{10}H_{12}^{2-}$ (Fig. 5).

---

‡ B_6H_8 has not been obtained, but $B_6H_6^{2-}$ does exist. Formally, protonation of the latter should yield B_6H_8, analogously to the reaction $B_{10}H_{10}^{2-} + 2H^{2+} \rightarrow B_{10}H_{12}$. [38]

§ Obtained for the isomer $C_2B_8H_{12}$. [40,41]

¶ A C-$\overset{+}{N}R_3$-substituted derivative of this carborane ($R_3NCB_9H_{11}$) has been obtained; the molecule is neutral as a result of the presence of the cationic fragment $R_3\overset{+}{N}$. [35]

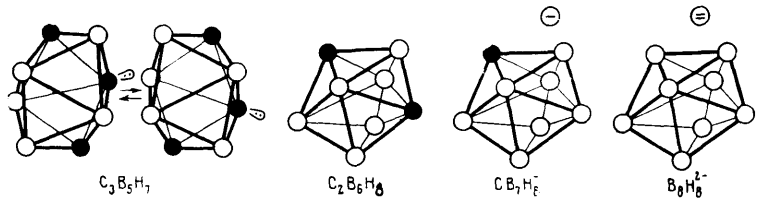


Figure 4.

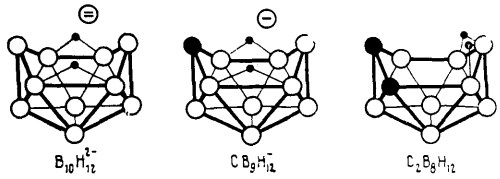


Figure 5.

The above isoelectronic series can be significantly extended by employing the atoms of other elements as the structural units of the polyhedral molecules, such as those of aluminium, gallium, zinc, germanium, tin, lead, nitrogen, phosphorus, sulphur, arsenic, and others.

Since the isoelectronic compounds have corresponding structures, it follows that carbon and other atoms are involved in the formation of the system of bonding orbitals in the same way as boron atoms, i.e. all the principles governing the formation of chemical bonds proposed for boron hydrides[4] apply to them. When transition metal atoms are considered as structural units, account must be taken of the specific character of their bonds with the carborane ligand. Transition metal complexes with carborane ligands have been examined in detail in Hawthorne's reviews[19,21-23].

3. The Three-centre Bond and the Influence of the Carbon Atom on Electron Distribution in Carboranes

The characteristics of the structure and chemical bonding in boron hydrides and carboranes have been explained by postulating the formation of a two-electron chemical bond between three atoms (a three-centre bond). In the non-excited state there are two electrons in the three-centre bonding orbital. In boron hydride and carborane molecules all the atomic orbitals of each atom are involved in the formation of a chemical bond and all the resulting bonding orbitals are filled with electrons. Three different types of three-centre bonds can be formed: the central B–B–B bond, the open B–B–B bond, and the open B–H–B bond.

In the central B–B–B bond each atom provides one hybridised atomic orbital, and the orbitals overlap in such a way that the maximum electron density is in the centre of the triangle (Fig. 6*a*). In the open B–B–B bond the central atom provides a *p* orbital and the other two supply hybridised atomic orbitals, their overlapping being of the type shown in Fig. 6*b*. In the open B–H–B bond the central hydrogen atom provides the *s* orbital for the formation of the bond and the two boron atoms provide their hybridised atomic orbitals (Fig. 6*c*). In case *a* 2/3 of an electron formally corresponds to each atom forming the three-centre bond, and in cases *b* and *c* there is one electron per central atom, while the other two atoms each have half an electron. The principles governing the calculation and description of the bonding in boron hydrides and carboranes have been described in detail in Lipscomb's monograph[4].

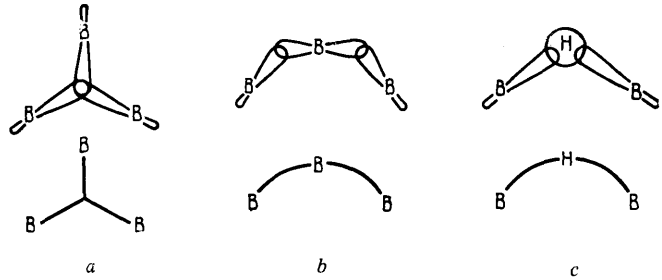


Figure 6.

When highly symmetrical $B_nH_n^{2-}$ anions and certain carboranes were considered, it proved convenient to describe these structures on the hypothesis that molecular orbitals delocalised over the entire molecule are present[43-46].

Using the Edmiston–Ruedenberg method, Lipscomb and coworkers recently determined the degree of localisation of the orbitals for a series of carboranes and introduced the concept of fractional three-centre bonds, i.e. essentially of specifically delocalised three-centre bonds embracing more than three atoms of the molecule[47-51]. It was shown that the valence structures of boron hydrides can be described without resorting to open three-centre B–B–B bonds[50,52]. For example, Fig. 7 illustrates the valence structure of decaborane[53], used until 1971 and proposed by Laws et al.[51] On the other hand, valence structures involving open three-centre B–C–B bonds were suggested for some of the carboranes investigated[50].

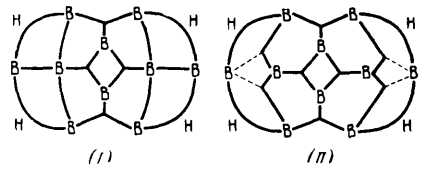


Figure 7.

Fig. 8 presents the valence structure proposed recently for the compounds 1,2-$C_2B_4H_6$,[50] 1,6-$C_2B_4H_6$,[50] 2,3-$C_2B_4H_8$,[49] and 2,4-$C_2B_5H_7$.[47,48]

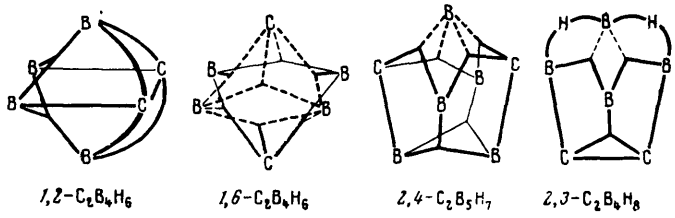


Figure 8.

Having surveyed the available data, Lipscomb and coworkers[50] formulated several additional conclusions the essential features of which are as follows:

(1) there exist unique valence structures for many boranes and carboranes (B_2H_6, B_4H_{10}, B_5H_{11}, B_6H_{10}, 1,2-$C_2B_4H_6$, 2,4-$C_2B_5H_7$, 2,3-$C_2B_4H_8$, etc.);

(2) the concept of fractional three-centre bonds can be successfully applied to certain boron hydrides and carboranes;

(3) for the description of boron hydrides, it is not obligatory to resort to the concept of the open B–B–B three-centre bond;

(4) in contrast to boron hydrides, the employment of the concept of the open three-centre bond in order to describe the valence structure is useful for only some carboranes.

Since the carbon atoms in carboranes are involved in the formation of three-centre and two-centre bonds, like boron atoms, and bearing in mind that the charge of the carbon nucleus is greater by unity than that of the boron nucleus, the appearance of an excess positive charge on the carbon atoms (at least in relation to the boron atoms equivalent in the structural sense) may be expected. The polyhedral species $B_nH_n^{2-}$ have a 2- charge and in a symmetrical structure, for example the icosahedral structure, the charge is distributed uniformly among all the boron atoms. The replacement of two BH structural units by two CH units leads to a molecule which is neutral as a whole. Two "superfluous" electrons remain (in $B_nH_n^{2-}$), but, instead of being localised, are distributed over the entire molecule. As a result, the carbon atoms bear a considerable positive charge.

Certain chemical properties of carboranes and of the functional groups linked to carbon atoms are due to the excess positive charge on the carbon atoms. This is manifested by the acidity of the hydrogen atoms in the C–H bonds, by the cleavage of the C–C and C–element bonds with substituents in certain functional derivatives of carboranes, by the ^{13}C NMR spectra, and by other physicochemical properties. This factor can also account for the electron-accepting effect of the corresponding carboranyl group in the carboranes investigated.

The presence of a positive charge on the carbon atom leads to the "withdrawal" of the electron densities from the neighbouring boron atoms, and these atoms of the carborane nucleus are in fact involved in nucleophilic reactions, while electrophilic reactions involve the boron atoms most remote from carbon[44,45].

The general ideas concerning the chemical reactions and their possible mechanisms are discussed in Section VI.

III. THE SYNTHESIS, STRUCTURE, AND PROPERTIES OF *CLOSO*-CARBORANES

Dicarba-*closo*-pentaborane(5) ($C_2B_3H_5$)

Of the three possible isomers of the first representative of *closo*-carboranes, two are known—1,2- and 1,5-$C_2B_3H_5$ (Fig. 9). According to a molecular orbital calculation, the thermodynamic stability of the $C_2B_3H_5$ carborane isomers decreases in the sequence 1,5->1,2->2,3-.[53] Among these isomers, 1,5-$C_2B_3H_5$ is the most readily available and has been most thoroughly investigated. For example, 1,2-$C_2B_3H_5$ was obtained by Grimes[54,55] in the form of the *CB*-dimethyl derivative in a mixture with other carboranes by the reaction of acetylene and diborane in an electric discharge. The structure with the methyl groups in the 2- and 3-positions has been proposed for this compound on the basis of ^{11}B NMR, ^1H NMR, infrared and mass-spectrometric data.

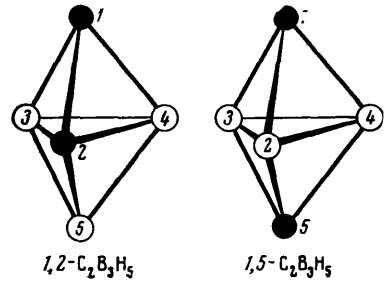


Figure 9.

The 1,5-$C_2B_3H_5$ isomer was detected in the pyrolysis products of a mixture of acetylene and diborane[3]. It is also formed, in a mixture with other carboranes, by the reaction of pentaborane(9) with acetylene in an electric discharge[26]. Methods have been developed for the synthesis of the lowest carboranes in high yields[56–58]. The interaction of pentaborane(9) and acetylene in a stream at 500–600°C using hydrogen as the carrier gas leads to a 70% yield of a mixture of the lower carboranes containing about 40% of 1,5-$C_2B_3H_5$.[56] Pyrolysis of 2,3-$C_2B_4H_8$ at 450–460°C for 10 s gives a 100% yield (25–30% conversion) of a mixture of the same carboranes containing 40% of 1,5-$C_2B_3H_5$.[57,58] The structure of the carborane was established on the basis of ^{11}B NMR, ^1H NMR, infrared and mass-spectrometric data[26]. The exact molecular structure of 1,5-$C_2B_3H_5$ was determined by electron diffraction[59].

1,5-$C_2B_3H_5$ is resistant to the action of air, water, carbon dioxide, and acetone at room temperature. Also at room temperature, the carborane mixed with B_2D_6 exchanges the hydrogen atoms linked to boron for deuterium[26]. The chemical stability of this compound can be explained by its high electronic symmetry. The breakdown of the symmetry following the introduction of polar substituents results in a decrease of stability[60]. For example, the adduct of 1,5-$C_2B_3H_5$ with triethylamine and the product of the halogenation of the carborane are stable only at a low temperature (−78°C). With increase of temperature, the compounds decompose. On the other

hand, derivatives of the carborane with non-polar substituents are stable. When, 1,5-$C_2B_3H_5$ is heated to 350°C in sealed tubes for 9 h, it dimerises with formation of a B–B bond between two $(C_2B_3H_4)_2$ bipyramids. The formation of a small amount of the trimer $C_2B_3H_4(C_2B_3H_3)C_2B_3H_4$ has also been suggested. The reaction of 1,5-$C_2B_3H_5$ with methylacetylene leads to an interesting result. *B*-(*cis*-prop-1-enyl)-1,5-dicarba-*closo*-pentaborane ($C_2B_3H_4$.C_3H_5)—the product of the addition of the *closo*-carborane to the acetylene derivative—is formed in 20% yield after 24 h at 165°C.[60] At 300°C, 1,5-$C_2B_3H_5$ interacts with diborane to form 3,6-$C_2B_6H_{10}$ in a yield less than 5%.[61]

Monocarba-*closo*-hexaborane(7) (CB_5H_7)

This compound is obtained in the decomposition of 1-methylpentaborane(9) in an electric discharge[62]. Another method of synthesis involves the pyrolysis of alkylpentaboranes(9).[63] According to ^{11}B NMR, ^1H NMR, and infrared spectroscopic data, CB_5H_7 has an octahedral structure (Fig. 10). It is of interest to note that the bridging hydrogen atom is not localised between two boron atoms, but executes tautomeric transitions with $\Delta G = 14$ and 12 kcal mole^{-1} for CB_5H_7 and $CH_3CB_5H_6$ respectively[63]. This is reflected in the ^{11}B NMR spectra, which contain three doublets with 1 : 2 : 2 intensity ratios at −30°C, while at 110°C the spectrum consists of two doublets with a 1 : 4 intensity ratio in consequence of the rapid transitions of the bridging hydrogen atom between the boron atoms in the 2-, 3-, 4-, and 5-positions, i.e. the boron atoms in these positions are indistinguishable by the above method. It is suggested that the tautomeric transitions take place via a transition state with a bridging hydrogen atom between the boron atoms in the 3- and 6-positions[63]. When acted upon by bases, the CB_5H_7 molecule splits off the bridging hydrogen atom with formation of the anion $CB_5H_6^-$.[64]

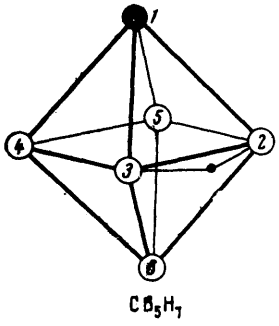


Figure 10.

Dicarba-*closo*-hexaborane(6) ($C_2B_4H_6$)

Both possible isomers of dicarba-*closo*-hexaborane with the carbon atoms in the 1,2- and 1,6-positions have been obtained (Fig.11). It is formed in a mixture with other carboranes by the reaction of acetylene with pentaborane in an electric discharge[65]. The analogous interaction of acetylene with diborane leads to a mixture of products containing 1,6-$C_2B_4H_6$.[54,55] The best method for the synthesis of a mixture of $C_2B_4H_6$ isomers on a preparative scale involves the decomposition of $C_2B_4H_8$ by ultraviolet radiation[66]. The yields of the 1,2- and 1,6-isomers in this reaction reach 15 and 20% respectively, with the simultaneous formation of 15% of 1,5-$C_2B_3H_5$. 1,2-$C_2B_4H_6$ is formed in a low yield (3–5%) in the pyrolysis of $C_2B_4H_8$ at 450°C in the course of 0.5 s; the yield of the 1,6-isomer in this reaction is about 20%.[57]

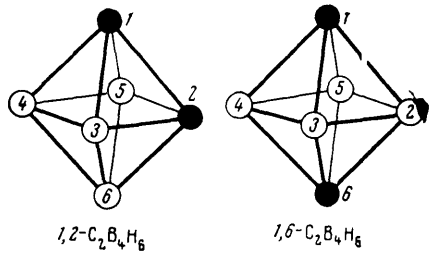


Figure 11.

An octahedral structure has been proposed for 1,2- and 1,6-$C_2B_4H_6$ on the basis of NMR, infrared spectroscopic, and mass-spectrometric data (Fig. 11).[27] The exact molecular structure of 1,6-$C_2B_4H_6$ in the gas phase was determined by electron diffraction[59,67]. The 1,2-$C_2B_4H_6$ [68] and 2-Cl-1,6-$C_2B_4H_5$ [69] structures were investigated by microwave spectroscopy. The results led the authors[69] to the conclusion that there is no additional interaction between the chlorine atom and the carborane nucleus, i.e. the contribution of B–Cl π bonding in 2-Cl-1,6-$C_2B_4H_5$ is almost zero.

The 1,6-isomer is thermodynamically more stable than the 1,2-isomer by 15 kcal mole^{-1} [70,71] and at 250°C the latter is converted quantitatively into 1,6-$C_2B_4H_6$.[72] Certain chemical properties of only one of the isomers (1,6-$C_2B_4H_6$) have been studied. The carborane is stable at room temperature in air and does not react with water or acetylene; it exchanges with B_2D_6 the hydrogen atoms bound to boron[27]. The reaction of 1,6-$C_2B_4H_6$ with a threefold excess of trimethylamine at room temperature in the course of eleven days leads to the formation of 5-Me_3N^+.$(2,4\text{-}C_2B_4H_6)^-$. The base introduces an additional electron pair into the nucleus of the *closo*-carborane and converts it into a *nido*-carborane derivative 2,4-$C_2B_4H_8$.[73] The dilithio-derivative $LiCB_4H_4CLi$ is formed slowly by the reaction 1,6-$C_2B_4H_6$ with BuLi in ether at room temperature; the dilithio-derivative reacts with MeI to form a *CC*-dimethyl derivative and treatment with one equivalent of MeI and then with bromine yields $MeCB_4H_4CBr$. The interaction with electrophilic agents proceeds via the boron atoms. Thus bromination in the presence of $AlBr_3$ gives rise to 2-Br-1,6-$C_2B_4H_5$,[74] while iodination in the presence of Al_2I_6 leads to the formation of 2-I-1,6-$C_2B_4H_5$.[75] Iodocarborane reacts with trimethylamine to form the quaternary ammonium salt $[Me_3N^+C_2B_4H_5]I^-$, which suggests the mobility of the I atom in the B–I bond.

Treatment of 1,6-$C_2B_4H_6$ with sodionaphthalene followed by the addition of $CoCl_2$ and NaC_5H_5 and oxidation with air led to a mixture of products, from which 1,7,2,4-$(CoC_5H_5)_2$.$C_2B_3H_5$ was isolated in 3% yield[76]. This complex is formally a derivative of the tetra-anion $C_2B_3H_5^{4-}$.

Dicarba-*closo*-heptaborane(7) ($C_2B_5H_7$)

In this case four isomers are possible of which only two (2,3- and 2,4-$C_2B_5H_7$) have been obtained (Fig. 12). The 2,3-isomer has been isolated in a yield of about 1.5% as the *CC*-dimethyl derivative from a mixture with other carboranes formed by the reaction of B_8H_{12} with dimethylacetylene. The structure of the compound has been determined by NMR and infrared spectroscopy[40].

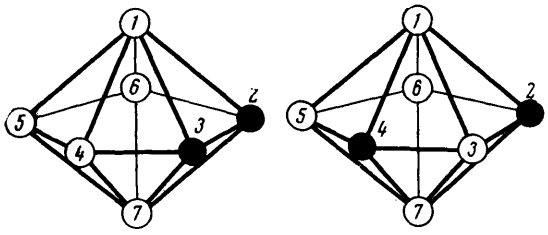


Figure 12.

The 2,4-$C_2B_5H_7$ isomer is more readily available and has been studied in greater detail. It was obtained for the first time by the reaction of B_5H_9 with acetylene in an electric discharge[26,27]. It is formed in 40% yield on pyrolysis of $C_2B_4H_8$ at 450°C for 10 s. Pyrolysis for 8 h above 300°C leads to a single volatile reaction product—2,4-$C_2B_5H_7$, in a yield reaching 38%.[57,58,77] This carborane is also formed together with other products from a mixture of diborane and acetylene in an electric discharge[54,55]. A structure has been proposed for 2,4-$C_2B_5H_7$ on the basis of NMR, infrared and mass-spectrometric data[77]. Subsequently the pentagonal bipyramidal structure was confirmed by microwave spectroscopy[78]. The study of the vibrational spectra of 2,4-$C_2B_5H_7$ and two other lower carboranes (1,5-$C_2B_3H_5$ and 1,6-$C_2B_4H_6$) led to the assignment of all the line frequencies, to the determination of the integral line intensities, and to the calculation of the polarisation constants[79].

The 2,4-$C_2B_5H_7$ isomer reacts with BuLi in ether to form the dilithio-derivative. *C*-Methyl, *CC*-dimethyl, *C*-bromo-, and *C*-trimethylsilyl derivatives of 2,4-$C_2B_5H_7$ were obtained from the lithio-derivatives. When the carborane is treated with alcoholic alkali, it undergoes total degradation[80]. Electrophilic reactions involve the boron atom in the 5-position. For example, bromination in the presence of $AlBr_3$ leads to 5-Br-2,4-$C_2B_5H_7$ [80] and chlorination yields 5-Cl-2,4-$C_2B_5H_7$.[81] A mixture of all the isomers (1-, 3-, and 5-$ClC_2B_5H_6$) is formed under the conditions of radical chlorination.

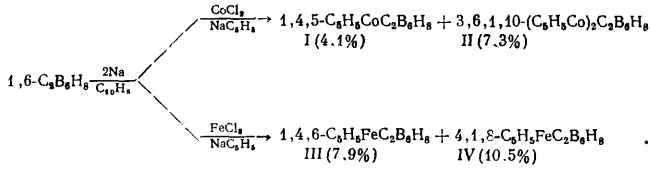
The hydrogen atoms linked to $B_{(3)}$, $B_{(5)}$, and $B_{(6)}$ are involved in isotope exchange with B_2D_6 at room temperature, and on heating to 100°C the hydrogen atoms at $B_{(1)}$ and $B_{(7)}$ are also exchanged[82].

When a solution of 2,4-$C_2B_5H_7$ in tetrahydrofuran (THF) is treated with sodionaphthalene and then with $CoCl_2$ and NaC_5H_5 and oxidised by air, a mixture of compounds is formed, eight of which have been isolated[83]. Two of these are derivatives of the dianion $C_2B_5H_7^{2-}$ and the tetraanion $C_2B_5H_7^{4-}$. In addition there are the mononuclear and dinuclear complexes $(C_5H_5)Co(C_2B_4H_6)$, $[(C_5H_5)Co]_2(C_2B_4H_6)$, $(C_5H_5)Co(C_2B_6H_8)$, and $[(C_5H_5)Co]_2(C_2B_6H_8)$, which are the products of the disproportionation of the polyhedral carborane ligand $C_2B_5H_7$. The mechanism of the disproportionation reaction has not been established.

Treatment of the reaction mixture obtained by reducing $C_2B_5H_7$ with $FeCl_2$ and NaC_5H_5 followed by oxidation leads to the preferential formation of 5-[(2)-2,4-$C_2B_5H_6$]-1,2,4-$C_5H_5Fe^{III}C_2B_4H_5$ and a small amount of 1,2,4-$C_5H_5Fe^{II}HC_2B_4H_6$ and 5-R-1,2,4-$C_5H_5Fe^{III}C_2B_4H_5$, where R = $C_{10}H_7H$ (traces). It is interesting to note that analogous iron complexes with a carborane ligand are formed directly from 2,4-$C_2B_5H_7$ and $Fe(CO)_5$ when they are heated in the gas phase. 1,2,4-$(CO)_3Fe^{III}C_2B_4H_6$ and 5,1,7-$(CO)_3Fe^{III}C_2B_5H_7$ were isolated[84].

Dicarba-*closo*-octaborane(8) ($C_2B_6H_8$)

Six structural isomers are possible. However, only the 1,6-$C_2B_6H_8$ isomer has so far been obtained. It was first isolated in a yield of about 12% as the *CC*-dimethyl derivative by the reaction of hexaborane(10) with dimethylacetylene[33]. The authors proposed a dodecahedral structure (Fig. 13) as the most likely. Hawthorne and coworkers synthesised this isomer in a mixture with other carboranes by the pyrolysis of $C_2B_7H_{13}$; the yield of 1,6-$C_2B_6H_8$ reaches 30%.[31,32,85] A method of synthesis based on the pyrolysis of $C_2B_5H_7$ in the presence of B_2H_6 has also been proposed[86]. The cleavage of 1,6-$C_2B_6H_8$ by Me_4NBH_4 on heating in diglyme with subsequent treatment by dry HCl leads to a mixture of the monocarba-*nido*-boranes CB_5H_9, 1-$MeCB_5H_8$, and 3-$MeCB_5H_8$.[87] The reduction of 1,6-$C_2B_6H_8$ with sodionaphthalene in THF followed by treatment with transition metal salts and NaC_5H_5 led to a series of transition metal π complexes with the carborane ligands C_2B_6:[88]



The reaction constants for the carboranyl group have been determined using *C*-(fluorophenyl)derivatives of 1,6-dicarba-*closo*-octaborane: $\sigma_i = +0.08$ and $\sigma_R^\circ = -0.02$.[89]

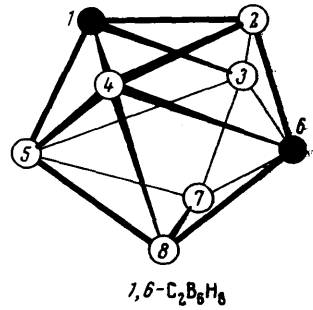
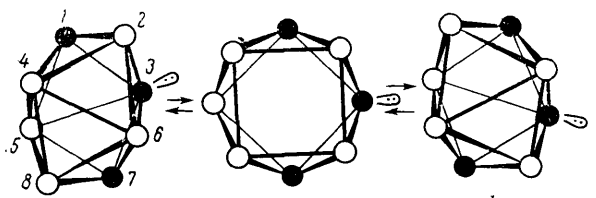


Figure 13.

Tricarba-*closo*-octaborane(7) ($C_3B_5H_7$)

$C_3B_5H_7$ is rightly regarded as one of the most interesting and unusual carboranes and is an example of tricarba-*closo*-boranes—compounds which, according to the isoelectronic principle, should be either positively charged or should exist in the form of neutral molecules with an overal zero charge as a result of the abstraction of a single proton from the carbon atom. Two carbon atoms differ from the third, at which there is a free electron pair.

The carborane $C_3B_5H_7$ was obtained by the pyrolysis of μ-SiH_3- or 4-SiH_3-2,3-$C_2B_4H_7$ in 15–20% yields [39]. According to ^{11}B NMR and ^1H NMR data, rapid transitions between structures *a* and *b* (Fig. 14) and time-averaged NMR spectra are observed. Thus the ^{11}B NMR spectrum contains three doublets with the intensity ratios 2 : 2 : 1 and the ^1H NMR spectrum contains three quartets due to the protons bound to boron and the signal due to the proton in the C–H bond with the relative intensity ratio 5 : 2. $C_3B_5H_7$ is stable in air and withstands heating to 250°C. On heating to 450°C, partial degradation takes place quantitatively, and 2,4-$C_2B_5H_7$ is formed. The fate of the carbon atom split off was not determined.



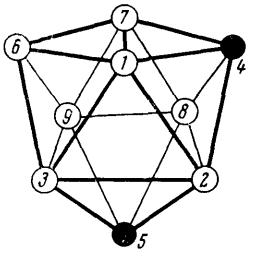
1,3,7-$C_3B_5H_7$

Figure 14.

Dicarba-*closo*-nonaborane(9) ($C_2B_7H_9$)

Six isomers are possible, but the only one known is 4,5-$C_2B_7H_9$ (Fig. 15), which is obtained by the pyrolysis of $C_2B_7H_{13}$ in a yield of about 7% [32,85] together with other carboranes. The yield of $C_2B_7H_9$ increases in the pyrolysis of the sodium salt of $C_2B_7H_{13}$. [85] 4,5-$C_2B_7H_9$ is also formed in a yield of 30% as a result of the slow reaction of 1,6-$C_2B_6H_8$ with B_2H_6 at room temperature [90]. The structure of the compound, proposed on the basis of infrared spectroscopic and NMR data [32,85], has been confirmed by the X-ray diffraction analysis of 4,5-$Me_2C_2B_7H_7$. [91]

As expected, electrophilic substitution of 4,5-$C_2B_7H_9$ involves the boron atom in the 6-position, it being most remote from the carbon atoms. 6-Me, 6-Et-, and 6-Br-4,5-$C_2B_7H_8$ have been obtained. The product of exhaustive bromination at 100°C is the tetrabromo-derivative [92] and not the pentabromide. The reduction of 4,5-$C_2B_7H_9$ by sodium in THF followed by treatment with $CoCl_2$ and NaC_5H_5 and oxidation by air leads to the formation of the three complexes 2,3,10-$C_5H_5CoC_2B_7H_9$ (I), 4,1,8-$C_5H_5CoC_2B_6H_8$ (II), and 1,2,3,6-$(C_5H_5Co)_2C_2B_8H_{10}$ (III). Compound (II) is the cobalt analogue of the iron–carborane complex 4,1,8-$C_5H_5FeC_2B_6H_8$. The complexes (I) and (III) are derivatives of the dianion $C_2B_7H_9^{2-}$ and the tetra-anion $C_2B_8H_{10}^{4-}$. $\sigma_i = 0.09$ and $\sigma_R^\circ = -0.05$ for the 4,4,5-$C_2B_7H_8$ group were determined using *C*-(fluorophenyl) derivatives. The authors believe that σ_R° for this group is higher than the corresponding constant for other carboranes [89].



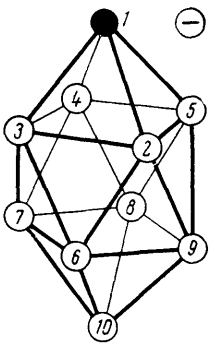
4,5-$C_2B_7H_9$

Figure 15.

Decahydromonocarba-*closo*-decaborate (1-) ($CB_9H_{10}^-$)

Two isomers are possible. One of them, 1-$CB_9H_{10}^-$ (Fig. 16), was obtained by the following reaction [93,42]:

$$Na_2B_{10}H_{13}CN \xrightarrow{2H^+} CB_{10}H_{12}NH_3 \xrightarrow[NaOH,\ H_2O]{Me_2SO_4} CB_{10}H_{12}NMe_2 \xrightarrow[Na,\ THF]{} CB_{10}H_{13}^- + 2\text{-}CB_{10}H_{11}^- \xrightarrow{310^\circ} 1\text{-}CB_9H_{10}^- + CB_{11}H_{12}^-.$$



1-$CB_9H_{10}^-$

Figure 16.

The electrochemical oxidation of $Et_4N^+CB_9H_{10}^-$ in acetonitrile involves dimerisation with formation of $(Et_4N^+)_2B_{18}C_2H_{18}^{2-}$. According to ^{11}B NMR data, the compound has a dimeric structure with a σ bond between the boron atoms in the 10- and 10′-positions [94]. Chlorination of $CB_9H_{10}^-$ in aqueous solution at room temperature yields $CB_9H_5Cl_5^-$. According to ^{11}B NMR data, the chlorination involves boron atoms remote from carbon. The chlorination of the dimer with formation of the *B*-octachloro-derivative proceeds similarly [94].

Dicarba-*closo*-decaborane(10) ($C_2B_8H_{10}$)

Of the seven possible isomers, three have been obtained: 1,2-, 1,6-, and 1,10-$C_2B_8H_{10}$ (Fig. 17). The 1,2-isomer can be synthesised in a nearly quantitative yield by the pyrolysis of 5,6-$C_2B_8H_{12}$ [95] or its sodium salt at 120–200°C *in vacuo*.[96] 1,2-$C_2B_8H_{10}$ is also one of the products of the thermal decomposition of $C_2B_7H_{11}$.[40] The structure of the carborane was established by infrared spectroscopy and NMR.[95,96] Among chemical properties, its capacity for involvement in oxidation and reduction reactions is noteworthy. When it is treated with sodium in THF, a dianion is formed and protonation of the latter gives 5,6-$C_2B_8H_{12}$ in 30% yield[96]:

$$1,2\text{-}C_2B_8H_{10} \xrightarrow{2e} (C_2B_8H_{10})^{2-} \xrightarrow{2H^+} 5,6\text{-}C_2B_8H_{12}.$$

The 1,6-$C_2B_8H_{10}$ isomer is formed on pyrolysis of $C_2B_7H_{13}$. When this reaction is carried out in the presence of diborane, the yield of 1,6-$C_2B_8H_{10}$ increases to 41%. About 8% of 1,7-$C_2B_{10}H_{12}$ is formed similarly. Other carboranes were not isolated[32,85]. When B_2H_6 is allowed to react with sodium salt of $C_2B_7H_{12}^-$ and $C_2B_7H_{13}$ in an ethereal solution, the yield of the isomer reaches 75–80%.[97]

Rapid pyrolysis of 5,6-$C_2B_8H_{12}$ at 500°C *in vacuo* gives a mixture of the two isomers 1,6-$C_2B_8H_{10}$ and 1,10-$C_2B_8H_{10}$.[96] Structures were proposed for 1,6- and 1,10-$C_2B_8H_{10}$ on the basis of infrared spectroscopic and NMR data[32,85] and have been confirmed by X-ray diffraction of 1,6-Me_2-1,6-$C_2B_8H_8$.[98] Among the three isomers of *closo*-$C_2B_8H_{10}$, the 1,10-isomer is the most stable. The 1,2- and 1,6-isomers are wholly converted into the 1,10-isomer on heating to 300°C. Among chemical properties, mention should be made of the fairly high acidity of the C–H protons, which are readily split off under the influence of strong bases (pK_a = 27.3 for the 1,10 isomer[99]). Interaction of 1,6- and 1,10-$C_2B_8H_{10}$ with BuLi results in the formation of the dilithio-derivative, from which various *C*-substituted carboranes were obtained[100–102]. Treatment of 1,6-$C_2B_8H_{10}$ with aqueous-alcoholic alkali leads to partial degradation of the carborane with elimination of the boron atom in the 2-position and the formation of $C_2B_7H_{12}^-$. The reaction with piperidine proceeds similarly.

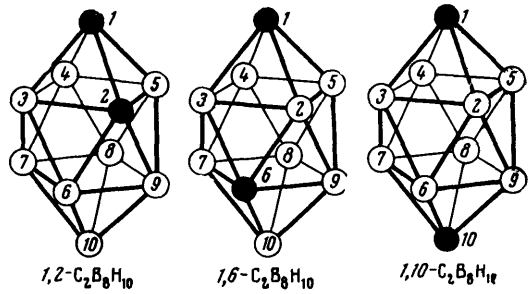


Figure 17.

Under the influence of acids, the 1,6-isomer decomposes to boric acid, and the reaction of 1,6-$C_2B_8H_{10}$ with diborane yields 1,7-$C_2B_{10}H_{12}$. The 1,10-$C_2B_8H_{10}$ isomer is resistant to the action of both acids and alkalis. Photochemical chlorination of 1,10-$MeC_2B_8H_8$ results in the formation of 1,10-$(CCl_3)_2C_2B_8Cl_8$.[100] The dianions derived from 1,6- and 1,10-$C_2B_8H_{10}$ form a wide range of complexes with transition metals[98,103].

σ_i = +0.10 and +0.05 and σ_R° = −0.02 and −0.01 have been determined for the 1,6-$C_2B_8H_9$ and 1,10-$C_2B_8H_9$ carbonyl groups. The results indicate a weak electron-accepting effect of these groups. The latter is enhanced on passing from a pentacoordinate to a hexacoordinate carbon atom (σ_R^- = +0.19 for the 1-1,7-$C_2B_{10}H_{11}$ group). When the carbon atoms are remote from one another, as in $C_2B_{10}H_{12}$, σ_R° diminishes[104].

Undecahydromonocarba-*closo*-undecaborate(1-) ($CB_{10}H_{11}^-$)

Five isomers are possible, of which only one, 2-carba-*closo*-undecaborate(1-), is known at present[42,93] (Fig. 18) The ^{11}B NMR spectrum of this isomer at 80.5 MHz consists of three doublets with the relative intensities 1 : 5 : 4. The authors suggest that the carbon atom is in the 2-position, the structure undergoing a rapid rearrangement via the *dsd* mechanism to an equivalent structure (Fig. 18). For this reason, the boron atoms in the 1-, 4-, 5-, and 8-positions and also in the 3-, 6-, 7-, 10-, and 11-positions are indistinguishable in the ^{11}B NMR spectra, while the atom in the 9-position gives rise to a signal with a relative intensity of unity[94]. It is noteworthy that another mechanism has been proposed for the isomerisation of 2-$CB_{10}H_{11}^-$ to account for the observed spectrum and has been used by Tolpin and Lipscomb[105] for $B_{11}H_{11}^{2-}$ (Fig. 19). If the "opening–closure" of the structure of 2-$CB_{10}H_{11}^-$ involves the atoms in the 1-, 4-, 5-, and 8-positions adjoining the carbon atom in the 2-position, the ^{11}B NMR spectrum should also show three doublets with the intensity ratios 1 : 5 : 4, referring to the boron atoms in the 9-position, the 3-, 7-, 6-, 10-, and 11-positions, and the 1-, 4-, 5-, and 8-positions respectively.

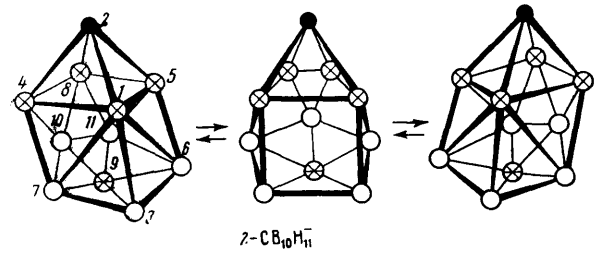


Figure 18.

Dicarba-*closo*-undecaborane(11) ($C_2B_9H_{11}$)

Of the 20 possible isomers of this carborane, only one (2,3-$C_2B_9H_{11}$) is known (Fig. 20); it is formed on pyrolysis of $C_2B_9H_{13}$ at 100°C in a yield of about 22%. Under the same conditions, the yield of the *CC*-dimethyl derivative from the corresponding dicarbaundecaborate reaches 75%.[32,106] A structure was proposed for $C_2B_9H_{11}$ on the basis of ^{11}B NMR and ^1H NMR data and the formation of the optically inactive $C_2B_9H_{10}Ph$ from the optically active

anion $C_2B_9H_{11}Ph^-$ (this shows that the plane of symmetry passes through the carbon atoms [107]). It was subsequently confirmed by X-ray diffraction [108].

Oxidation of 2,3-$C_2B_9H_{11}$ by iron(III) salts or $H_2Cr_2O_7$ in aqueous solutions results in partial decomposition of the initial carborane with formation of $C_2B_7H_{13}$. [32,109] Treatment of 2,3-$C_2B_9H_{11}$ in benzene at 0°C with chromic acid leads to the "oxidative hydroxylation" product 4,5-$(OH)_2$-2,3-$C_2B_9H_9$. [110]

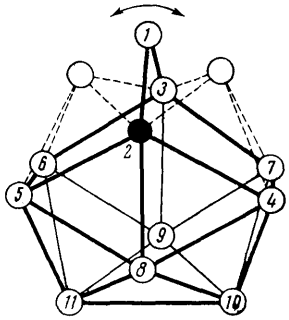


Figure 19.

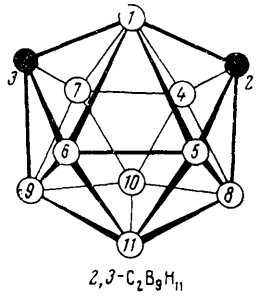


Figure 20.

Nucleophilic agents react with $C_2B_9H_{11}$ to form adducts of the type $C_2B_9H_{11}L$. [106,111,112] The interaction of 2,3-$C_2B_9H_{11}$ with a number of Lewis bases (L) leads to the opening of the *closo*-carborane structure and the formation of 10-L-7,9-$C_2B_9H_{11}^-$. Bu^-, Me^-, H^-, malonic acid derivatives, and the carboranyl anions $C_2B_8H_9^-$ and $C_2B_{10}H_{11}^-$ have been used as L. [111] However, the reaction with other Lewis bases, such as EtO^-, PPh_3, and NMe_3, results in the formation of a 3-substituted derivative 3-L-7,9-$C_2B_9H_{11}$. [112] The formation of 10-substituted dicarbaundecaborate anions in one case and of 3-substituted derivatives in the other may be associated, according to the authors [112], with the fact that, on being attacked by L, the boron atom in the 1-position in $C_2B_9H_{11}$ moves in one case to the side opposite to that from which the Lewis base attacks, with formation of the isomer 10-L-7,9-$C_2B_9H_{11}$, while in the other case the boron atom moves in the opposite direction and 3-L-7,9-$C_2B_9H_{11}$ is formed (Fig. 21). However, we believe that this explanation is inadequate (see Section VI).

2,3-$C_2B_9H_{11}$ interacts with two equivalents of sodium in THF, the second equivalent adding on only in the presence of naphthalene and treatment of the reaction mixture with $CoCl_2$ and NaC_5H_5 followed by oxidation with air results in the formation of a mixture of complexes [88]. $\sigma_i = +0.12$ and $\sigma_R^\circ = +0.01$ for the 2-$C_2B_9H_{10}$ carbonyl group [114,115].

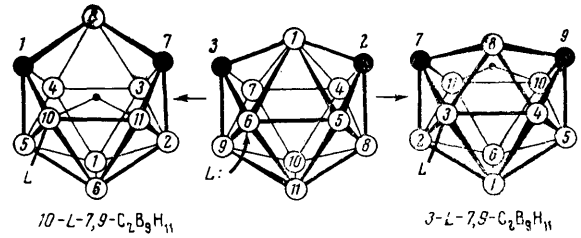


Figure 21.

Dodecahydromonocarba-*closo*-dodecaborate(1-) ($CB_{11}H_{12}^-$)

The only possible isomer $CB_{11}H_{12}^-$ (Fig. 22) is formed together with $CB_9H_{10}^-$ from cyanodecaborane [93,42]. A structure was proposed for the carborane on the basis of the ^{11}B NMR spectrum, which contains three doublets with the relative intensities 1 : 5 : 5. The carborane is not oxidised at the anode in acetonitrile up to a potential of 2.4 V. [94]

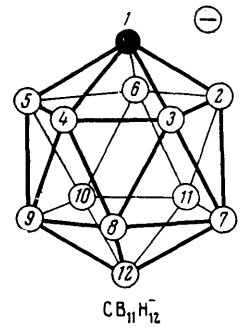


Figure 22.

Dicarba-*closo*-dodecaborane(12) ($C_2B_{10}H_{12}$)

All three possible isomers, 1,2-, 1,7-, and 1,12-$C_2B_{10}H_{12}$, are known (Fig. 23). Since there are very numerous data for the properties of the $C_2B_{10}H_{12}$ isomers, we shall consider only their most general properties. More detailed information can be found in a number of reviews [2,3,15,113].

The thermodynamic stability of the carborane(12) isomers varies in the series $o > m \sim p$.

$$1,2\text{-}C_2B_{10}H_{12} \xrightarrow{450^\circ} 1,7\text{-}C_2B_{10}H_{12}. \quad (1)$$

$$1,7\text{-}C_2B_{10}H_{12} \xrightleftharpoons{600^\circ} 1,12\text{-}C_2B_{10}H_{12} \quad . \quad (2)$$

At a high temperature an equilibrium mixture of the *m*- and *p*-isomers is formed [116] [Eqn.(2)]. Under the influence of strong bases, protons are readily abstracted at room temperature from the carbon atoms with formation of the corresponding carboranyl anions.

The p*K*a, determined by various methods for the *o*-, *m*-, and *p*-isomers, are respectively 19, 24, and 26 (Kashin et al.[117]) and 23.3, 22.9, and 30 (Petrov et al.[118]). Hawthorne and coworkers showed that treatment with alkalis under severe conditions results in the cleavage of the *o*- and *m*-carborane nuclei with formation of 1,2- and 1,7-$C_2B_9H_{12}^-$.[30,119] 1,12-$C_2B_{10}H_{12}$ undergoes a similar cleavage in low yield to 2,9-$C_2B_9H_{12}$ only in a 20% KOH solution in boiling propanediol. Protonation of this anion leads to the non-polar compound 2,9-$C_2B_9H_{13}$.[120]

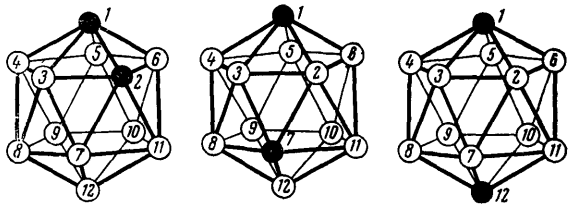


Figure 23.

The stability of the carborane(12) isomers varies in the sequence $o < m < p$. The interaction of derivatives containing one or two alkali metal and alkaline earth metal atoms with electrophilic agents leads to *C*-derivatives. Electrophilic substitution takes place at the boron atoms most remote from the carbon atoms. Substitution in 1,2-$C_2B_{10}H_{12}$ takes place primarily in the 9(12)-position; the 1,7-isomer is substituted in the 9(10)-position and the 1,12-isomer in the 2-position, the only one possible. The ease and rates of electrophilic reactions of the three carborane isomers also vary in the sequence $o > m > p$.

The oxidation of the $C_2B_{10}H_{12}$ isomers by $KMnO_4$ in an acid medium leads to the formation of all the possible *B*-hydroxy-derivatives[121]. Reduction with sodium in liquid ammonia or THF leads to dianions[122] and the oxidation of the dianion obtained from 1,12-carborane(12) gives rise to 1,7-carborane(12), while the oxidation of the dianions derived from 1,7- and 1,2-carboranes(12) leads to the formation of 1,2-carborane(12).[123,124] Treatment of the dianions with $CoCl_2$ or other transition metal salts and NaC_5H_5 results in the formation of complexes where the metal atom constitutes the thirteenth vertex of the polyhedron[125,126]. Protonation of the dianions leads to the dicarbadodecaborate(1-) monoanions. The structures of some of these have been determined by X-ray diffraction[127,128]. The molecular structures of *o*-, *m*-, and *p*-$C_2B_{10}H_{12}$ have been determined by electron diffraction[129]. $\sigma_I = +0.295$ and $+0.213$, and $\sigma_R^0 = +0.004$ and -0.036 have been found for the fluorophenyl derivatives of the corresponding 1,2- and 1,7-carborane isomers respectively[114].

IV. THE SYNTHESIS, STRUCTURE, AND PROPERTIES OF *NIDO*- AND *ARACHNO*-CARBORANES

1. *NIDO*-CARBORANES

Dicarbo-*nido*-pentaborane(7) ($C_2B_3H_7$)

Three isomers of $C_2B_3H_7$ are possible. The only one of these obtained, 1,2-$C_2B_3H_7$, was isolated after the reaction of the tetraborane(10) B_4H_{10} with acetylene in the gas phase at 50°C. Its structure (Fig. 24) is based on ^{11}B and ^1H NMR data[130]. The carborane is stable in the gas phase at 50°C, but decomposes at 100°C. In the liquid state polymerisation with formation of $(C_2B_3H_7)_X$ takes place at temperatures as low as 25°C. The polymerisation is greatly accelerated in the presence of HCl, polar solvents, and other polar substances. In dilute non-polar solutions this compound is comparatively stable. The schemes quoted below illustrate its chemical properties[131]:

$$C_2B_3H_7 + C_2H_2 \xrightarrow{50^\circ} C_4B_2H_6 + \text{solid residue}\ .$$

To determine the characteristics of the formation of $C_4B_2H_6$, the reaction of $C_2B_3H_7$ with acetylenic compounds labelled with deuterium and ^{13}C was investigated. It was shown that the alkyne is inserted preferentially in the C–B bond and to a lesser extent in the C–C bond[132].

$$C_2B_3H_7 + C_2H_4 \xrightarrow{90^\circ} BEt_3 + B_2H_2Et_4;$$
$$C_2B_3H_7 + BMe_3 \rightarrow B_5H_8 + H_2 + \text{solid residue};$$
$$C_2B_3H_7 + NEt_3 \rightarrow C_2B_3H_7 \cdot NEt_3;$$
$$C_2B_3H_7 + NaH \rightarrow \text{polymerisation};$$
$$C_2B_3H_7 + Br_2 \rightarrow Br_2C_2B_3H_7 \xrightarrow{Br_2} BBr_3 + HBr + \text{solid residue}.$$

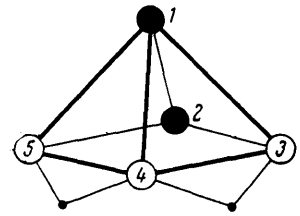


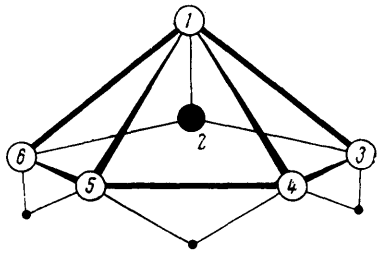
Figure 24.

1,2-$C_2B_3H_7$ reacts with iron pentacarbonyl to form a π complex[131]. The reaction of $(\pi\text{-}C_2B_3H_7)Co(\pi\text{-}C_5H_5)$, an analogue of $(\pi\text{-}C_2B_3H_7)Fe(CO)_3$, with sodium hydride, followed by treatment with $CoCl_2$ and NaC_5H_5, results in the formation of a complex of the type $[(\pi\text{-}C_5H_5)Co]_2.(\pi\text{-}C_2B_3H_5)$, which is an example of a dinuclear complex with three parallel planar ligands[76].

Monocarba-*nido*-hexaborane(9) (CB_5H_9)

Of the two possible isomers of this carborane, only the 2-CB_5H_9 isomer with the carbon atom at the base of a pentagonal pyramid is known (Fig. 25). This compound is

one of the products of the pyrolysis of methylpentaborane[63]. 2-Et-2-CB_5H_8 is formed in 3.3% yield by the reaction of pentaborane with lithium methylacetylide[133]. Methyl derivatives of 2-CB_5H_8 are also formed as side products in the synthesis of 2,3-$C_2B_4H_8$.[134] The fully alkylated monocarba-*nido*-hexaborane(9) ($MeCB_5H_3Me_5$) is a side product in the reaction of acetylene with tetraethyldiborane[135,136]. The structure of CB_5H_9, proposed on the basis of ^{11}B NMR data[137,138], was confirmed by microwave spectroscopy[139]. Pyrolysis of CB_5H_9 at 250°C for 3.5 days leads to 1,7-$C_2B_{10}H_{12}$ and $C_2B_7H_{13}$.[140] This method of synthesis of the higher carboranes from the lower carboranes is of definite theoretical interest†.



2-CB_5H_9

Figure 25.

Dicarba-*nido*-hexaborane(8) ($C_2B_4H_8$)

Three isomers of this carborane are possible, two of which have been obtained (Fig. 26). A derivative of 2,4-$C_2B_4H_8$ has been synthesised, namely the ammonium inner salt $C_2B_4H_7^-N^+Me_3$ (see p.647).[73] The second isomer 2,3-$C_2B_4H_8$ can be synthesised and is well known. It is formed in a yield of about 40% in the pyrolysis of a mixture of pentaborane(9) and acetylene at 235°C for 40 h.[72] The structure of the carborane, proposed on the basis of ^{11}B NMR, ^1H NMR, and infrared spectroscopic data[34,72,141], was confirmed by the X-ray diffraction of its *CC*-dimethyl-derivative[142,143]. The vibrational spectra of the unsubstituted and *C*-methyl-substituted carboranes have been published and discussed[144]. Pyrolysis of 2,3-$C_2B_4H_8$ leads to a mixture of the lowere *closo*-carboranes, the process being the most convenient method for the synthesis of the *closo*-carboranes $C_2B_3H_5$, $C_2B_4H_6$, and $C_2B_5H_7$.[57,58,77] The electrophilic halogenation of 2,3-$C_2B_4H_8$ and its *C*-methyl derivatives involves the boron atoms adjoining the carbon atoms at the base of the molecule[145,146]. This mode of reaction is inconsistent with the charges calculated by the SCF method, according to which electrophilic reactions should involve the boron atom in the 1-position. To account for the above course of reaction, Marynick and Lipscomb[49] carried out a comparative assessment of the bonding orbitals in the molecule and demonstrated the considerable role of the orbitals of the skeleton in the reaction (see Section VI).

† Rietz and Hawthorne[140] suggest that 1,2-$C_2B_{10}H_{12}$ can be obtained from 2,3-$C_2B_4H_8$ and B_6H_{10} and that the composition of the products formed from B_6H_{10}, $C_3B_3H_7$, and $C_4B_2H_6$ should be investigated.

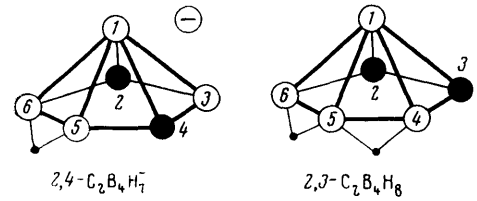


Figure 26.

Isotope exchange between 2,3-$C_2B_4H_8$ on the one hand, and D_2 and B_2D_6 on the other has been studied and various deuterio-derivatives of this carborane have been obtained[147]. When an ethereal solution of $C_2B_4H_8$ is treated with sodium hydride, the product is dicarba-*nido*-hexaborate(1-) anion ($C_2B_4H_7^-$),[148] which reacts with alkyl halide derivatives of silicon, germanium, boron, lead, tin, and also with chlorosilane and chlorogermane to give the corresponding bridged derivatives, in which the atom of the element is linked by a three-centre bond with two boron atoms of the carborane[149,151]. The interaction of SiH_2Cl_2 with two equivalents of $C_2B_4H_7^-$ in THF at 0°C leads to a 70% yield of a compound with two carborane ligands bound to the SiH_2 group by two three-centre bonds—$\mu\mu'$-$SiH_2(C_2B_4H_7)_2$ (Fig. 27).[151,152] The compounds obtained with an MR_3 or MR_2 bridge group containing non-transition elements are good examples illustrating the possibility of the formation of a non-classical chemical bond not only by boron atoms but also by a number of non-electron-deficient elements, including carbon (see Section VI).

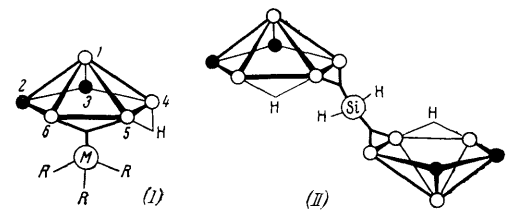


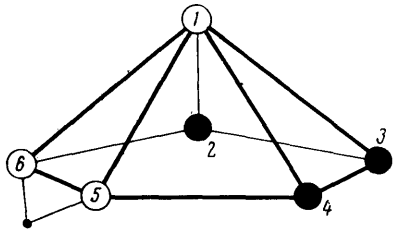
Figure 27.

The reaction of $Na^+C_2B_4H_7^-$ with $(\pi\text{-}C_5H_5)Fe(CO)_2I$ initially leads to a complex in which iron is bounded by a three-centre bond to the carborane ligand, namely μ-[$(\pi\text{-}C_5H_5)$.$Fe(CO)_2$]$C_2H_4B_7$; this compound can be converted in 90% yield into the π complexes $(\pi\text{-}C_5H_5)Fe^{II}(\pi\text{-}C_2B_4H_7)$ and $(\pi\text{-}C_5H_5)Fe^{III}(\pi\text{-}C_2B_4H_6)$.[84,153] The interaction of Na^+.$C_2B_4H_7^-$ with NaC_5H_5 and $CoCl_2$ in THF with subsequent oxidation by air leads to 1,7,2,3-$(C_5H_5Co)_2C_2B_3H_5$.[76] The reaction of 2,3-$C_2B_4H_8$ with an excess of $Fe(CO)_5$ at 240°C also leads to π complexes of the transition metal with carborane ligands. 1,2,3-$(CO)_3FeC_2B_4H_6$ and 1,2,3-$(CO)_3FeC_2B_3H_7$ were obtained by this reaction[84,154]

Tricarba-*nido*-hexaborane(7) ($C_3B_3H_7$)

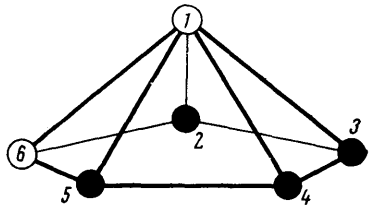
Of the four possible isomers, only one (2,3,4-$C_3B_3H_7$) has been obtained (Fig. 28). *C*-Methyl derivatives of this carborane are formed at 50°C in the gas-phase reaction

between tetraborane(10) (B_4H_{10}) with acetylene. The yields of the methyl derivatives 2-$MeC_3B_3H_6$ and 2,3- and 2,4-$Me_2C_3B_3H_5$ are respectively 3.3, 6.5, and 5.3%.[155,156] The interaction of B_4H_{10} with C_2H_2 is a first-order reaction with respect to B_4H_{10} and a zero-order reaction with respect to acetylene. The proposed reaction mechanism involves the formation of B_4H_8 in the first, slowest stage, and this compound then interacts rapidly with acetylene, giving a solid polymeric residue $(C_2BH_4)_x$ (80%) and a mixture of volatile products, in which 4-$MeCB_5H_8$, 2,3-$C_2B_4H_8$, and 2,3,4-$C_3B_3H_7$ are also present in an overall yield of 2%.[156] In many studies the mechanism of the formation of tricarbohexaborane (7) and its methyl derivatives was studied using C_2D_2.[156,157] When 2,4-$Me_2C_3B_3H_5$ and other $C_3B_3H_7$ derivatives are treated with strong bases, a proton is abstracted from the bridging position with formation of the corresponding anions. Treatment of these anions with DCl leads to μ-D-derivatives of $C_3B_3H_7$.[157,158] Treatment of the anion 2-$MeC_3B_3H_5^-$ with pentacarbonylmanganese bromide leads to an adduct, where Mn is linked to a σ bond to the boron atom of the carborane ligand according to the authors[153]. When the adduct is heated, two equivalents of CO are evolved and 2Me-1,2,3,4-$(CO)_3MnC_3B_3H_5$ is formed. Heating of 2-$MeC_3B_3H_6$ and 2,3-$Me_2C_3B_3H_6$ with $Mn_2(CO)_{10}$ in the gas phase leads to similar complexes[158].



2,3,4,-$C_3B_3H_7$

Figure 28.



2,3,4,5-$C_4B_2H_6$

Figure 29.

Tetracarba-*nido*-hexacarborane(6) ($C_4B_2H_6$)

This compound completes the family of the *nido*-carboranes $CnB_6-nH_{10}-n$ having the structure of a pentagonal pyramid. Of the three possible isomers, only one has been obtained, in which all the carbon atoms are located at the base of the pyramid (Fig. 29). The fully alkylated carborane was synthesised according to the scheme[159]

$$NaR_3BC \equiv CR + ClBR_2 \rightarrow R_2BRC = CRBR_2 \rightarrow C_4B_2R_6.$$

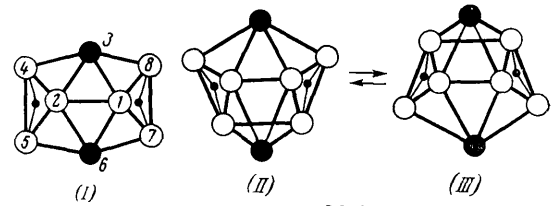
The unsubstituted carborane $C_4B_2H_6$ was obtained by the pyrolysis of 1,2-tetramethylenediborane[63]. The carborane is also formed in 5–10% yield in the reaction of $C_2B_3H_7$ with C_2H_2.[131,132] Its structure was established by ^{11}B NMR, ^1H NMR, infrared[63,159,160] and microwave[161] spectroscopy. According to the authors[161], $C_4B_2H_6$ can be regarded as an analogue of the π complexes of the cyclopentadienyl anion in which one of the carbon atoms at the base and the transition metal atom have been replaced by two boron atoms, but this similarity is extremely formal.

Dicarba-*nido*-octaborane(10) ($C_2B_6H_{10}$)

Of the seven possible isomers, only one (3,6-$C_2B_6H_{10}$) has been obtained (Fig. 30). Its yield in the reaction of $C_2B_3H_5$ with diborane is less than 5%:

$$C_2B_3H_5 + {}^3/_2B_2H_6 \xrightarrow{300^\circ} C_2B_6H_{10} + 4H_2.$$

It is suggested that, under the reaction conditions, B_3H_7 is formed from B_2H_6 and reacts with $C_2B_3H_5$ to give $C_2B_6H_{10}$.[61] The low yield of this carborane is probably due to its instability. Thus in the liquid state 3,6-$C_2B_6H_{10}$ decomposes with formation of mainly $C_2B_6H_8$ and $C_2B_5H_7$. 3,6-$C_2B_6H_{10}$ is the first carborane isoelectronic with B_8H_{12}. The structure (I) of the compound was established on the basis of ^{11}B and ^1H NMR data. The authors[61] also do not rule out the possibility of tautomeric transitions between the equivalent structures (II) and (III) (Fig. 30). They also quote the interatomic distances in the molecule[61].



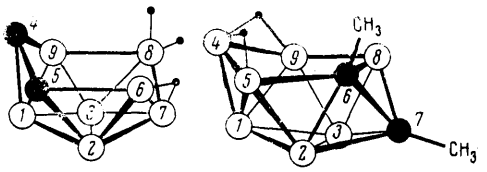
3,6-$C_2B_6H_{10}$

Figure 30.

Dicarba-*nido*-nonaborane(11) ($C_2B_7H_{11}$)

This carborane can have 25 isomers depending on the position of the carbon atoms in the molecule. The reaction of octaborane(12) (B_8H_{12}) with acetylenic compounds gives an approximately 65% yield of a mixture of two *nido*-carboranes with seven and eight boron atoms in the molecule[40,162]. The unsubstituted carborane $C_2B_7H_{11}$ is interesting because, according to ^{11}B NMR, ^1H NMR, and infrared spectroscopic data, one of the boron atoms, in the 8-position, is linked by σ bonds to two hydrogen atoms, i.e. this compound is the first example of a carborane containing the BH_2 group (Fig. 31).[161] It is striking that the *CC*-dimethyl derivative of this carborane, obtained by the

reaction of B_8H_{12} with dimethylacetylene, has a structure different from that of the unsubstituted $C_2B_7H_{11}$ (Fig. 31), which is shown clearly by the ^{11}B and ^1H NMR spectra[181]. X-Ray diffraction[163] confirmed the structure proposed for $Me_2C_2B_7H_9$ on the basis of ^{11}B NMR, ^1H NMR, and infrared spectroscopy[40]. The structural differences and the greater stability of the *CC*-dimethyl derivative of $C_2B_7H_{11}$ have been explained by the steric or electronic influence of the methyl groups[162].

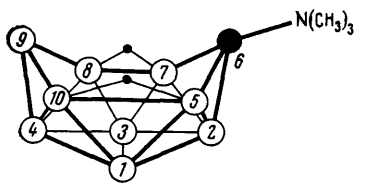


4,5-$C_2B_7H_{11}$ 6,7-$(CH_3)_2$-$C_2B_7H_9$

Figure 31.

Monocarba-*nido*-decaborane(13) ($C_1B_9H_{13}$)

Four isomers of $C_1B_9H_{13}$ are possible, of which only the 6-CB_9H_{13} isomer, obtained in the form of the derivative $B_9H_{11}CNMe_3$, is known (Fig. 32). The structure of this carborane was established on the basis of ^{11}B NMR, ^1H NMR, and infrared spectroscopic data[42].



6-$N(CH_3)_3$-CB_9H_{11}

Figure 32.

Dicarba-*nido*-decaborane(12) ($C_2B_8H_{12}$)

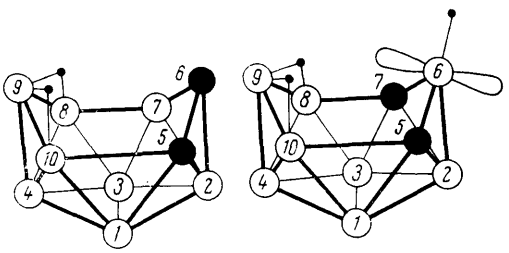
Of the sixteen possible isomers of $C_2B_8H_{12}$, two have been obtained: 5,6- and 5,7-$C_2B_8H_{12}$ (Fig. 33). As already mentioned, the 5,6-$C_2B_8H_{12}$ isomer is the main product of the reaction of octaborane(12) (B_8H_{12}) with acetylene. The *CC*-dimethylderivative is obtained by the analogous reaction with dimethylacetylene. A structure has been proposed for the carboranes on the basis of ^{11}B NMR, ^1H NMR, and infrared spectroscopic data and also the fact that the decomposition of the *CC*-dimethyl derivative in propionic acid on a palladium catalyst results in the formation of n-butane[40,162]. 5,6-$C_2B_8H_{12}$ is also formed in 90% yield in the oxidation of 7,8-$C_2B_9H_{12}$ by Fe^{3+} in an acid medium at 20°C in the course of 4 h.[95] As already mentioned, heating of the 5,6-isomer in *N*-ethylpiperidineborane yields 1,2-$C_2B_8H_{10}$.[95] Certain other reactions of 5,6-$C_2B_8H_{12}$ have been described[99]:

$$5,6\text{-}C_{12}B_8H_{12} \xrightarrow[\text{vacuum}]{500^\circ} 1,6\text{-} + 1,10\text{-}C_2B_8H_{10};$$

$$5,6\text{-}C_2B_8H_{11}^- \xrightarrow{120\text{–}200^\circ} 1,2\text{-}C_2B_8H_{10} + C_2B_8H_{10}^{2-} + H_2;$$

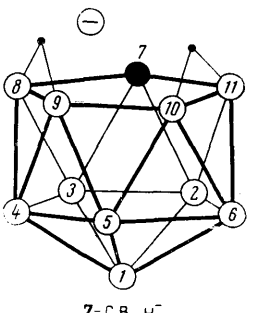
$$5,6\text{-}C_2B_8H_{12} + 2e \rightarrow C_2B_8H_{12}^{2-} \xrightarrow[H_3O^+]{200^\circ} 5,7\text{-}C_2B_8H_{10}^{2-} \rightarrow C_2B_7H_{13}.$$

The interaction of 5,6-$C_2B_8H_{12}$ with EtO^- gives a low yield of a new compound of the class of *arachno*-carboranes—6,9-$C_2B_8H_{14}$.[36] Another isomer, 5,7-$C_2B_8H_{12}$ (Fig. 33), was obtained by the reaction of $C_2B_7H_{12}^-$ with diborane[41]. According to the authors[41], the boron atom in the 6-position in this compound is *sp*-hybridised, one *p* orbital remaining free. In the interaction with trimethylamine this orbital and the orbital with the electron pair of the nitrogen atom form the B—N bond. When $C_2B_8H_{12}NMe_3$ is heated to 150°C, *closo*-1,6-$C_2B_8H_{10}$ is formed and treatment with anhydrous HCl in CH_2Cl_2 at 80°C gives rise to the initial carborane—5,7-$C_2B_8H_{12}$. Furthermore, treatment with an excess of HCl results in the substitution of the hydrogen atom in the 6-position by chlorine and the formation of 6-Cl-5,7-$C_2B_8H_{11}$, the carborane containing, like the unsubstituted compound, a free *p* orbital. Pyrolysis of the chlorocarborane *in vacuo* leads to *closo*-Cl-1,6-$C_2B_8H_9$ and treatment with D_2O yields $C_2B_7H_{11}D_2$, deuterium being linked to carbon atoms[41].



5,6-$C_2B_8H_{12}$ 5,7-$C_2B_8H_{12}$

Figure 33.



7-$CB_{10}H_{13}^-$

Figure 34.

Monocarba-*nido*-undecaborane(14) ($C_1B_{10}H_{14}$)

Among the three possible isomers, the derivatives of only one isomer, with the carbon atom in the open face, have been obtained (Fig. 34). The anion derived from this carborane ($CB_{10}H_{13}^-$) can be obtained either from cyanodecaborane[42,93] or by the reaction of decaborane with alkyl isocyanides[42,93,164-167]. Among the chemical properties of $C_{10}H_{13}^-$, electrophilic halogenation reactions have been mentioned. The reaction with Br_2 leads to mono- and di-bromo-derivatives. At 0°C chlorine decomposes this anion. The reaction with iodine does not occur even in the presence of catalysts. In electrophilic halogenation reactions $R_3NCB_{10}H_{12}$ is less reactive[167]; for example, bromination takes place only in the presence of $AlCl_3$. Numerous *C*- and *B*-derivatives of $CB_{10}H_{13}^-$ have been described[42]. π Complexes with transition metals have been obtained from $CB_{10}H_{11}^{3-}$ and $H_3NCB_{10}H_{10}^{2-}$.[42]

Dicarba-*nido*-undecaborane(13) ($C_2B_9H_{13}$)

Of the nine possible isomers, two compounds with the carbon atoms in the open face and the isomer with the carbon atoms in the 2,9-positions have been synthesised[120] (Fig. 35). 7,8-, 7,9-, and 2,9-$C_2B_9H_{13}$ are obtained on protonation of the corresponding dicarbaundecaborate anions, which are synthesised by the alkaline cleavage of 1,2- 1,7-, and 1,12-$C_2B_{10}H_{12}$. Structures have been proposed for the carboranes and their anions on the basis of ^{11}B NMR, ^1H NMR, and infrared spectroscopic data[30,31,32,106,119,120]. The 7,9-isomer is much less stable than the 7,8-isomer[32].

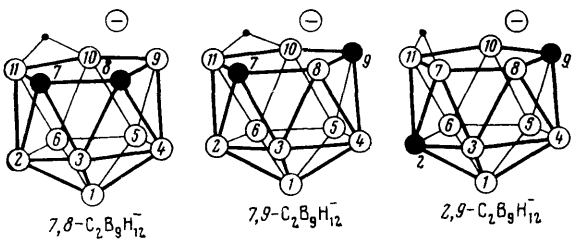


Figure 35.

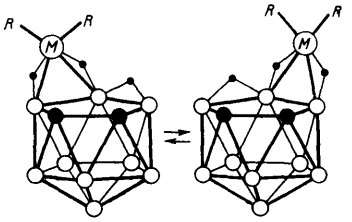


Figure 36.

The thermal decomposition of these carboranes, leading to *closo*-2,3-$C_2B_9H_{11}$, has already been mentioned[31,32]. The interaction of 7,8-$C_2B_9H_{13}$ with trialkylaluminium and trialkylgallium leads to $R_2Al.C_2B_9H_{12}$ and the corresponding gallium derivatives[168]. According to ^{11}B and ^1H NMR, the $AlMe_2$ group undergoes tautomeric transitions between two equivalent positions (Fig. 36).[169] X-Ray diffraction confirmed the conclusion that the $AlMe_2$ group is in the "bridging" position[170]. Heating of *nido*-$B_9C_2H_{12}MR_2$ (M = Al or Ga) in benzene leads to *closo*-1,2,3-$RMC_2B_9H_{11}$. On heating to 450°C, these compounds isomerise to a metallocarborane with the carbon atoms in the *m*-positions.

The reactions of both *nido*- and *closo*-metallocarboranes with $TiCl_4$ result in the formation of catalysts resembling Ziegler catalysts, in the presence of which ethylene polymerises at 25°C and 1 atm.[168] 7,8-$C_2B_9H_{13}$ can be titrated as a strong monobasic acid[30,32] and under the influence of strong bases the second bridge proton is also abstracted[119].

The structure of dicarba-*nido*-undecaborate(1-) anions was determined on the basis of ^{11}B NMR, ^1H NMR, and infrared spectroscopic data. The hydrogen atom in the bridge position in 7,8-$C_2B_9H_{12}$ undergoes rapid tautomeric transitions between the 9,10- and 10,11-positions. In 7,9-$C_2B_9H_{12}$ the bridge hydrogen atom is linked to the atoms in the 10- and 11-positions. The isotope exchange involving 7,8- and 7,9-$C_2B_9H_{12}^-$ and their derivatives has also been studied[171]. Comparison of the spectra of various 7,8-$C_2B_9H_{12}$ derivatives led to the assignment of the peaks in the ^{11}B NMR spectrum of this anion[171,172]. 7,9-$C_2B_9H_{12}$ is thermodynamically more stable than the 7,8-isomer and on heating to 300°C the latter is converted into the former[119,173].

The electrophilic substitution reactions of 7,8-$C_2B_9H_{12}^-$ take place at the open face with formation of 9-substituted derivatives of 7,8-$C_2B_9H_{11}^-$. For example, iodination with I_2 in an aqueous ethanol solution yields 9-I-7,8-$C_2B_9H_{11}^-$. The oxidative substitution reaction leads to the 9- and 10-substituted derivatives of the 7,8-isomer[174,175]. Alkylation of 7,9-$C_2B_9H_{11}^{2-}$ yields 10-Alk-7,9-$C_2B_9H_{11}^-$ (Fig. 37).[176]

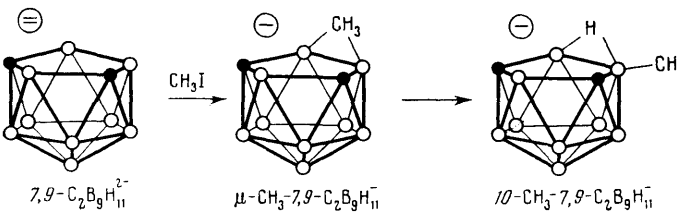
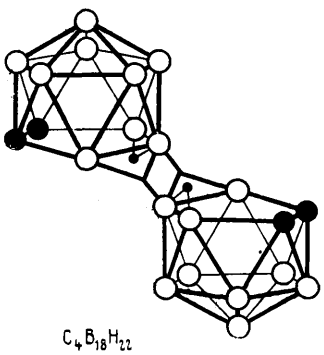


Figure 37.

Oxidation of 7,9-$C_2B_9H_{12}^-$ with chromic acid results in the formation of $C_2B_7H_{13}$ in a high yield[177]. Cautious oxidation of 7,8-$C_2B_9H_{12}^-$ in an acid medium at −15°C with $K_2Cr_2O_7$ leads to the stable carborane $C_4B_{18}H_{22}$. ^{11}B NMR, ^1H NMR, and infrared and ultraviolet spectroscopic data indicate a structure in which two $C_2B_9H_{11}$ fragments are joined by two three-centre bonds (Fig. 38).[178] As already mentioned, the oxidation of 7,8-$C_2B_9H_{12}^-$ by iron(III) salts in an acid medium leads to 5,6-$C_2B_8H_{12}$.[95] Numerous transition metal complexes were obtained with the dicarbollide ions $C_2B_9H_{11}^{2-}$.[2,19-23,179] The interaction of 7,8-$C_2B_9H_{11}^{2-}$ with GeI_2, $SnCl_2$, and $Pb(OAc)_2$ leads to heteroanalogues of tricarba-*closo*-dodecaborane(11).[180] ^{119}Sn Mössbauer spectroscopic data for 3-Sn-1,2-$C_2B_9H_{11}$ have

shown that the outer electronic shell of the tin(II) atom is of the $5s^2$ type [181]. The analogous germanium compound was obtained from 7,9-$C_2B_9H_{11}^{2-}$. The reaction of 7,9-$C_2B_9H_{11}^{2-}$ with $SnCl_2$ results in the formation of 2,3-$C_2B_9H_{11}$. 3-Sn-1,7-$C_2B_9H_9$ is formed as an intermediate [112]:

$$7,9\text{-}C_2B_9H_{11}^{2-} + SnCl_2 \rightarrow (3\text{-Sn-}1,7\text{-}C_2B_9H_{11}) \rightarrow 2,3\text{-}C_2B_9H_{11}.$$



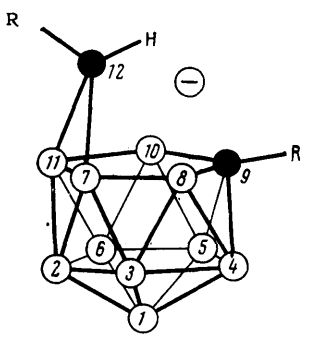
$C_4B_{18}H_{22}$

Figure 38.

The interaction of the dicarbollide ions with $RBCl_2$ leads to the restoration of the icosahedral structure, involving the formation of 3-R-$C_2B_{10}H_{11}$. [182-185] σ_i and σ_R^o have been determined for 7,8- and 7,9-$C_2B_9H_{12}^-$ and the corresponding dicarbollide ions [114,186]. Zakharkin et al. [186] believe that the second negative charge in $C_2B_9H_{11}^{2-}$ is located mainly at the boron atoms not in the open face.

Dicarbarba-*nido*-dodecaborane(14) ($C_2B_{10}H_{14}$)

The neutral compound have not been obtained. The anions of the corresponding *nido*-carboranes are formed when the dianions $(C_2B_{10}H_{12})^{2-}$ obtained from 1,2-, 1,7-, and 1,12-$C_2B_{10}H_{12}$ are protonated [187]. The structure of one of the $C_2B_{10}H_{13}^-$ isomers, based on X-ray diffraction data, is presented in Fig. 39. [127,128]



$R_2C_2B_{10}H_{11}^-$
(R=CH_3,C_6H_5)

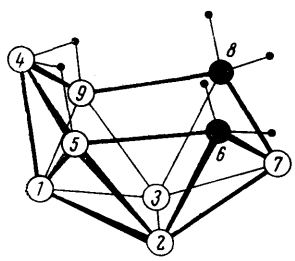
Figure 39.

2. *ARACHNO*-CARBORANES

arachno-Carboranes have the general formula $C_{0-6}B_nH_{n+6}$. This class of carboranes has been least thoroughly investigated. Only two *arachno*-carboranes have been obtained hitherto. They have an open structure, like *nido*-carboranes, and differ only by the number of hydrogen atoms in the open face. The most objective feature characterising *closo*, *nido*-, and *arachno*-carboranes is the electronic structure of compounds of these classes (see Section V).

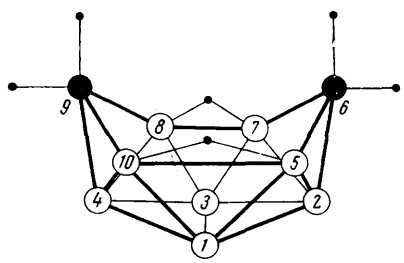
Dicarba-*arachno*-nonaborane(13) ($C_2B_7H_{13}$)

$C_2B_7H_{13}$ can have nineteen isomers. As already mentioned, the only one obtained (6,8-$C_2B_7H_{13}$) is formed as a result of the oxidation of $C_2B_9H_{11}$ in aqueous solution [32,35] or by the oxidation of 7,9-$C_2B_9H_{12}^-$ with chromic acid [177]. The structure of $C_2B_7H_{13}$ (Fig. 40) was established on the basis of ^{11}B NMR, ^1H NMR, and infrared spectroscopic data and also the study of the chemical properties of this carborane [32,35]. X-Ray diffraction data have been published for *CC*-$Me_2C_2B_7H_{11}$. [188] As already stated, thermal decomposition leads to a mixture of the *closo*-carboranes $C_2B_6H_8$, $C_2B_7H_9$, and $C_2B_8H_{10}$. [32,85] Interaction with strong bases leads to the abstraction of two "axial" protons from the carbon atoms with formation of $C_2B_7H_{11}^{2-}$, whose treatment with D^+ yields $C_2B_7H_{11}D_2$. [32] The interaction of $C_2B_7H_{11}^{2-}$ with $CoCl_2$ leads to the formation of π complexes containing two $C_2B_7H_9^{2-}$ carborane ligands with carbon atoms in the 1,6- or 6,9-positions, depending on the reaction conditions. The 1,10-isomer has been obtained by thermal isomerisation [189]. The reactions of $C_2B_7H_{11}^{2-}$ with $Mn(CO)_5Br$, $Mn_2(CO)_{10}$, and $Mn(CO)_2Cl$ in THF lead to 1,4,6-$(CO)_3MnC_2B_6H_8^-$. [190]



6,8-$C_2B_7H_{13}$

Figure 40.



6,9-$C_2B_8H_{14}$

Figure 41.

6,9-Dicarba-*arachno*-decaborane(14) ($C_2B_8H_{14}$)

As already mentioned, this carborane is formed when 5,6-$C_2B_8H_{12}$ is acted upon by EtO^-. Its structure has been proposed on the basis of ^{11}B NMR, ^1H NMR, and infrared spectroscopic data (Fig. 41).[36]

V. THE CHARACTERISTIC FEATURES OF THE VARIATION OF THE PHYSICOCHEMICAL PROPERTIES OF CARBORANES

The experimental data on the properties of *closo*-, *nido*- and *arachno*-carboranes which have accumulated can be treated in general terms and make it possible to discover a relation between their structure and the variation of their physicochemical and chemical properties in the light of the characteristics of the three-centre bonds in these compounds. The Table lists certain physicochemical parameters of carboranes, such as the interatomic distances l, the C–H bond stretching vibration wavenumbers ν(C–H), the chemical shifts of the C–B bond protons τ, and the coordination numbers (C.N.) of the carbon and boron atoms. When the interatomic distances in carboranes and other similar structures are compared, a striking feature is the greater distances between the atoms of the molecular skeleton compared with the bond lengths in classical organic and organoboron compounds. For example, the C–C distance in 1,2-$C_2B_{10}H_{12}$ is 1.65 Å,[129] which greatly exceeds l_{C-C} for the σ bond in organic compounds of different types ($l_{C-C} \leq 1.55$ Å).[194] The B–C distance in the same carborane is of the order of 1.71 Å [129] and in the 1,7-isomer it is 1.73 Å, while in trimethylboron the C–B bond length is 1.578 Å.[195] The greater C–C and B–C interatomic distances in carboranes undoubtedly reflect the specific nature of the bonds in these compounds. Evidently the increase of the C–C and B–C interatomic distances is associated with the deficiency of electrons and the specific features of the three-centre bond. In contrast to the bonds in the skeleton, where in the general case two-centre bonds also do not coincide with the straight line joining the two atoms, the external C–H and B–H bonds as well as the bonds with the substituents are ordinary σ bonds. As a result of this, comparison of the characteristics of these bonds with the behaviour familiar in organic chemistry and the chemistry of organic derivatives of the elements can yield useful information about the state of the atoms constituting the molecular skeleton. In organic compounds the C–H and C–Me bond lengths are known to depend on the hybrid state of the carbon atoms, amounting to 1.09 and 1.54 Å (sp^3), 1.07 and 1.49–1.53 Å (sp^2), and 1.06 and 1.46 Å (sp) respectively. The C–H and C–Me bond lengths in *closo*-carboranes are of the order of 1.1 and 1.53 Å, the corresponding values in *nido*-carboranes being 1.07 and 1.51 Å respectively. Comparison of these results (see Table) indicates the predominant sp^3 hybridisation of the carbon atoms in the majority of *closo*-carboranes‡ and sp^2 hybridisation in *nido*-carboranes. The shorter C–Me and particularly C–Hal bond lengths are in many cases apparently associated with the appreciable electron-accepting properties of the carbonyl groups. For example, the C–I bond length in 1,12-I_2-1,12-$C_2B_{10}H_{11}$ is 2.082 Å,[196] while in MeI it amounts to 2.132 Å;[194] on the other hand, in CF_3I the bond length is 2.101 Å.[197]

‡ In many cases, for example in the 1,6-$C_2B_8H_{10}$ molecule, carbon atoms are apparently in the sp^2 hybrid state.

Bearing in mind the σ bonding with the substituent, the state of the boron atoms in the polyhedron can be inferred also from the properties of the substituents linked to the polyhedron (H, halogen, alkyl, etc.); however, the lack of adequate experimental data still precludes such a comparison. Molecular orbital calculations indicate sp^3 or sp^2 hybridisation[4,24], while in the theory of three-centre orbitals an sp^3 hybrid state of the boron atoms is postulated[4]. Despite the insufficiency of experimental data, certain conclusions about the characteristics of the state of the boron atoms can be reached from a formal comparison of the coordination number with the possible distribution of electron density among the atoms of the polyhedron. Thus it is easy to note a tendency towards an increase of the distance between the atoms of the polyhedron with increase of the coordination number. An interesting approach to this problem was proposed by Wade in relation to the borane anions $B_nH_n^{2-}$. On the basis of the fact that the bond in *closo*-structures is formed by the $(n+1)$th electron pair [198], the author determined the formal number of electrons corresponding to each edge of the polyhedron, i.e. the "bond order" between the atoms as a function of n and the number of adjacent atoms (x_1 and x_2)§:

$$\text{"bond order"} = \frac{(n+1)(x_1+x_2)}{nx_1x_2}.$$

He attributed the decrease of the interatomic distance with decrease of the coordination number to the increase of the "bond order". Since the observed decrease of the interatomic distance is greater than expected, Wade concluded that in the given molecule the electronic charge is distributed non-uniformly, being higher on atoms with a lower coordination number than on atoms with a higher coordination number [199].

Evidently the absence of a direct relation between the interatomic distances and the coordination number can be explained if one considers the distribution of the $(n+1)$th electron pair over the localised bonding orbitals rather than over the atoms of the polyhedron. Each atom supplies three atomic orbitals for the formation of the bonds in the nucleus, i.e. is involved in the formation of three bonding orbitals, and the number of electrons joining the central atom to its x neighbours is six. Thus the formal number of electrons corresponding to the given atom will decrease with increase of the coordination number. The higher thermodynamic stability of the isomer of the given carborane in which the carbon atoms have a smaller coordination number¶ can be attributed to the fact that in these isomers the excess positive charge on the carbon atoms (see Section II) is more compensated compared with the isomers in which the carbon atoms have higher coordination numbers.

With increase of the number of atoms n forming the polyhedron (in consequence of the decrease of the quantity $n + 1/n$—the average number of electron pairs at each atom of the polyhedral molecule), there is an increase of the excess positive charge on the atoms of the polyhedron, including the carbon atoms with identical coordination numbers, which is manifested in the properties of the C–H bonds (see Table).

§ x = C.N. – 1, i.e. the outer σ bond is disregarded.

¶ In all the known unsubstituted carboranes the carbon atoms occupy the positions with the minimum coordination numbers. If several isomers of the given carborane are known, then the isomers in which the carbon atoms have a higher coordination number are converted into isomers with a smaller number coordination number[3], for example 1,6-$C_2B_8H_{10}$ → 1,10-$C_2B_8H_{10}$.[32]

In his study of the relation between the individual classes of carboranes, boron hydrides, and related structures, Wade noted that n-atomic molecules with *closo*-, *nido*-, and *arachno*-structures have respectively $n + 1$, $n + 2$, and $n + 3$ electron pairs binding together the molecular skeleton. The addition of an electron pair to the *closo*-structure $B_nH_n^{2-}$ leads to the *nido*-structure $B_nH_n^{4-}$ with a rearrangement of the skeleton and the formation of a fragment of the next polyhedron with one vertex missing[198]. Having combined with two electrons, the molecules of *closo*-carboranes are converted to the electronic analogues of *nido*-carboranes, corresponding to the *nido*-structures of derivatives of carborane dianions, and having combined with four electrons they are converted into analogues of *arachno*-carboranes. The addition of one proton per unit negative charge gives rise to structural analogues of *nido*- and *arachno*-carboranes[200]. For example:

$$2,3\text{-}C_2B_9H_{11} \xrightarrow{2e} C_2B_9H_{11}^{2-} \xrightarrow{H^+} 7,9\text{-}C_2B_9H_{12}^-\ ,$$
$$1,2\text{-}C_2B_8H_{10} \xrightarrow{2e} C_2B_8H_{10}^{2-} \xrightarrow{2H^+} 5,6\text{-}C_2B_8H_{12}\ .$$

Characteristics of carboranes.

Carborane	C.N.* C B	(C.N. of C)** l_{C-R}, Å (R = H, Me)	l_{C-C}, Å	(C.N. of C) l_{C-B}, Å (C.N. of B)**	(C.N. of B) l_{B-B}, Å (C.N. of B)**	^{1}H NMR spectrum*** τ_{C-H}, p.p.m.	i.r.(Raman) spectrum ν_{C-H}, cm^{-1}	σ_i; σ_R°	References****
closo-1,5-$C_2B_3H_5$	4 5	1.071	—	(4) 1.556(5)	(5) 1.853 (5)	5.35	3165 (3152)	—	26[bc], 59[a], 79[c]
1,2-$C_2B_4H_6$	5 5	1.10	1.540	(5) 1.605—1.627 (5)	(5) 1.721;1.752 (5)	—	—	—	27[bc], 68[a]
1,6-$C_2B_4H_6$	5 5	1.103; 1.11	—	(5) 1.633;1.635 (5)	(5) 1.720;1.725 (5)	7.63	3107 (3118)	—	27[bc], 59[a], 67[a], 79[c]
2,4-$C_2B_5H_7$	5 5;6	1.09	—	C(2)–B(3) 1.606 C(2)–B(6) 1.502	(5) 1.650 (5) (5) 1.650—1.894 (6)	— 4.3	3110 (3096)	—	77[bc], 78[a], 79[c]
1,7-$C_2B_6H_8$	5;6 5	—	—	—	—	5.2	3080	+0.08 −0.02	32[bc], 85[bc] 191[a], 89[d]
1,7-$Me_2C_2B_6H_6$	5;6	1.521	—	(5) 1.500 (5) (5) 1.595—1.697(6)	(5) 1.696—1.806 (6) (6) 1.842—1.920 (6)	7.84	2930	—	
4,5-$C_2B_7H_9$	5 5;6	—	—	—	—	4.4	3075	+0.09 −0.05	32[bc], 85[bc], 91[a], 89[d]
4,5-$Me_2C_2B_7H_7$	5 5;6	1.53	—	(5) 1.61(6)	(5) 1.72(6) (6) 1.77—2.01 (6)	7.5	2935	—	
1,6-$C_2B_8H_{10}$	5;6 5;6	—	—	—	—	(5)4.8;(6)8.1	3120,3070	+0.10 −0.02	32[bc], 85[bc], 98[a], 104[d]
1,6-$Me_2C_2B_8H_8$	5;6 5;6	(5) 1.505; (6) 1.527	—	(5) 1.588—1.611(6) (6) 1.632(5) (6) 1.750—1.777 (6)	(5) 1.681—1.696 (5) (6) 1.780—1.861(6)	(5)7.2;(6)8.7	3005,2960	—	
2,3-$C_2B_9H_{11}$	5 6;7	—	—	—	—	4.2	3060	+0,12 −0.01	32[bc] 108[a], 114[d] 115[d]
2,3-$Me_2C_2B_9H_9$	5 6;7	1.52	—	(5)1.60—1.70(6) (5)1.67(*l*)	(6)~1.80(6) 6) 2.05(*l*)	—	2885	—	
1,2-$C_2B_{10}H_{12}$	6 6	1.15	1.65	(6)~1.711(6)	(6) 1.793(6)	6.5	3080	+0.295 +0.004	129[a], 192[b], 114[d]
1,7-$C_2B_{10}H_{12}$	6 6	1.15	—	(6)~1.726(6)	(6) 1.805 (6)	7.15	3071	+0.213 −0.036	129[a], 192[b],
1,12-$C_2B_{10}H_{12}$	6 6	1.15	—	(6) 1.710 (6)	(6) 1.772—1.792 (6)	7.32	3067	—	129[a], 192[b]
nido-2-CB_9H_9	4 5; 6	—	—	(4) 1.530 (5) (4) 1.713 (6)	(5) 1.759—1.782 (6) (6) 1.781—1 830 (6)	4.62	—	—	137[a], 138[b], 139[b]
2,3-$C_2B_4H_8$	4 5;6	1.04	1.418	(4) 1.509 (5) (4) 1.748 (6)	—	—	3040,3032 (3044,3032)	—	34[b], 77[b], 144[c], 142[a] 143[a]
2,3-$Me_2C_2B_4H_6$	4 5;6	1.506	1.432	(4) 1.520 (5) (4) 1.762 (6)	(5) 1.768 (6) (6) 1.705 (6)	7.97	2980,2954, 2922 (2960,2927, 2869)	—	34[b]
2,3,4,5-$C_4B_2H_8$	4 4;6	—	C(2)–C(3) 1.436 C(3)–C(4) 1.424	(4) 1.541 (4) (4) 1.703 (4)	(4) 1.886 (2)	4.24 5.38	2950	—	63[bc], 159[bc], 160[bc] 161[a]
3,6-$C_2B_6H_{10}$	4 4;6	—	—	(5) 1.617 (5) (5) 1.697 (6)	(5) 1.704 (6) (6) 1.721 (6)	—	2975,2965 2878,2865	—	61[ac]
4,5-$C_2B_7H_{11}$	4;5 5;6	—	—	—	—	7.19;8,05	3048,2982	—	162[bc], 163[a]

Table (continued).

Carborane	C.N.* C B	(C.N. of C)** l_{C-R}, Å (R = H,Me)	l_{C-C}, Å	(C.N. of C)l_{C-B}, Å (C.N. of B)**	(C.N. of B)l_{B-B}, Å (C.N. of B)**	^{1}H NMR spectrum*** τ_{C-H}, p.p.m.	i.r.(Raman) spectrum ν_{C-H}, cm^{-1}	σ_I; σ_R^0	References****
6,7-$Me_2C_2B_7H_9$	5 5;6	1.47—1.53	1,55	(5) 1.60—1.75 (5) (5) 1.60—1.65 (6)	(5) ~1.80 (6) (6) 1.69—1.81 (6)	7.68;8.72	2965.2935	—	162bc, 163a
9,12-$C_2B_{10}H_{13}^-$	4;5 5;6	—	—	—	—	7.48;6.79 (doublet) 7.19 (doublet)	—	—	187b, 128a, 193b
9,12-$Me_2C_2B_{10}H_{11}^-$	4;5 5;6	(5) 1.520; (4) 1.518 C(12)— —H 0.957	—	(4) 1.642(6) (5) 1.625 (5) (5) 1.670 (6)	(5) 1.72—1.867(6) (6) 1.757—1.847 (6)	6.45(quartet) 8.32 (singlet) 8.67(doublet)	—	—	
arachno-6,8-$C_2B_7H_{13}$	5 5;6	—	—	—	—	9.9; 10.77	3055.2910	—	32bc
6,8-$Me_2C_2B_7H_{11}$	5 5;6	C—H 0.98 C—Me 1.527	—	(5) 1.700 (5) (5) 1.671—1.714 (6)	(5) 1.732 (6) (6) 1.710—1.826 (6)	8.7; 10.73	2925	—	188a

*The coordination numbers (C.N.) of carbon atoms (upper figures) and boron atoms (lower figures) are quoted.

**The coordination numbers of the atoms in the skeleton for which the interatomic distances are quoted are indicated in brackets.

***$\tau = 10 - \delta$; the coordination numbers of the corresponding carbon atoms are indicated in brackets for 1,6-$C_2B_8H_{10}$.

****a—interatomic distances; b—^{1}H NMR data; c—infrared and Raman spectroscopic data; d—reaction constants.

VI. THE POSSIBLE MECHANISMS OF THE CHEMICAL REACTIONS OF CARBORANES

The nature of the chemical bond in carboranes and boron hydrides is manifested not only in the characteristics of their structure but naturally also in the nature of their chemical reactions, such as reduction, oxidation, and interaction with nucleophilic and electrophilic agents. We shall attempt to consider the reactions involving localised three-centre as well as two-centre bonds.

1. Reduction of Carboranes

One of the most general and interesting reactions of carboranes, mainly *closo*-carboranes, is their ability to combine with electrons when acted upon by alkali metals. The addition of electrons to *closo*-structure with n-atoms in the polyhedron is accompanied by a rearrangement of the carborane molecule, the resulting anions being isolated in the form of transition metal complexes or protonation products with the metal atom inserted at the missing vertex of the polyhedron with $n + 1$ atoms.

In the light of ideas concerning three-centre bonds, the addition of two electrons can be formally represented as follows. The electrons can add on successively to the three-centre bond with formation of a two-centre bond and an atomic orbital with an electron pair. At the intermediate stages of their transfer electrons can be accommodated at a non-bonding orbital, if such is present, or at the nearest antibonding orbital (Fig. 42). Next, the system of bonding orbitals probably rearranges with formation of two two-centre orbitals, from the atomic orbital with the electron pair and a second three-centre orbital. Thus two three-centre orbitals are formally rearranged

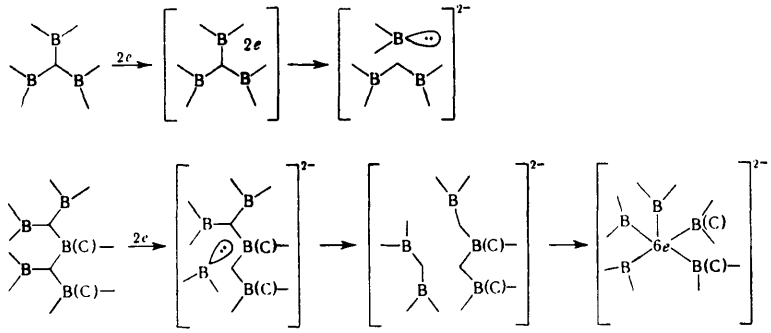


Figure 42.

into three two-centre orbitals, and the electron pair is located in the resulting additional bonding orbital. The bonding two-centre orbitals formed are probably to some extent delocalised, i.e. there is a possibility of the formation of (three) bonding five-centre orbitals, made up of the atomic orbitals of the atoms in the open face (Fig. 42). The last structure in Fig. 42 does not reflect the real directions of the atomic orbitals but merely the possibility of the formation of bonding orbitals common to the atoms in the open face (by analogy with Hawthorne's ideas concerning the nature of the bond in transition metal complexes with the carborane ligands $C_2B_9H_{11}^{2-}$ and in the dicarbollide ions themselves [179]).

The scheme in Fig. 42 illustrates the proposed mechanism of the addition of electrons to the *closo*-carborane molecule (a fragment of the possible valence structure is indicated). Two of the five atoms are carbon atoms. The scheme shows that the addition of electrons is accompanied by the opening of the structure, with formation of a pentagonal face. The possibility of the opening of the carborane nucleus with formation of a hexagonal face is illustrated by the scheme in Fig. 43. [201] Similarly to the scheme in Fig. 42, two of the six atoms are carbon atoms. It is noteworthy that the addition of electrons to the carborane molecule must involve primarily the immediate environment of the carbon atoms (the site with the lowest electron density) and in the resulting anions the carbon atoms must be located in the open face—the site with the maximum electron density. Accordingly, electrophilic reactions, for example protonation and interaction with transition metal salts (formation of metallocarboranes), proceed at the open face containing at least one carbon atom.

Substituents in the carborane nucleus may play an important role in determining the sites of addition of electrons. Depending on the nature of the substituent and its location in the polyhedron, the attack by electrons can take place at three-centre bonds other than in the unsubstituted carboranes. Furthermore, polarisation of the three-centre bond itself under the influence of the substituent can lead to the opening of the three-centre bond and hence of the polyhedral molecule in different directions, i.e. to the formation of an atomic orbital with an electron pair at different atoms of the polyhedron. All these factors lead to different sets of dynamic structures [201].

The addition of electrons must be accompanied by a considerable increase in the energy of the bonding orbitals of the carborane nucleus and the corresponding decrease of the energy of the antibonding orbitals. This must facilitate the corresponding rearrangements of the molecular skeleton. The rearrangements can lead either to a superposition of the physicochemical characteristics of the individual isomers or, when they are sufficiently rapid, to an averaging of the spectroscopic physicochemical parameters of the dianions in solutions [201].

The high reactivity of the dianions is shown also by the ease of occurrence of various chemical reactions, such as disproportionation, interaction with various electrophilic agents, with the solvent, etc. Thus, when electrons add to $2,4\text{-}C_2B_5H_7$, with subsequent treatment by $CoCl_2$ and NaC_5H_5 and then oxidation by air, a mixture of compounds is formed, eight of which have been isolated [83]. When the dianions are treated with transition metal salts, the resulting complexes have different structures [88], probably owing to the different electronic structures of the transition

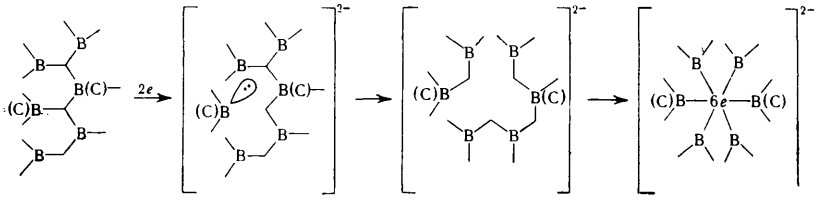


Figure 43.

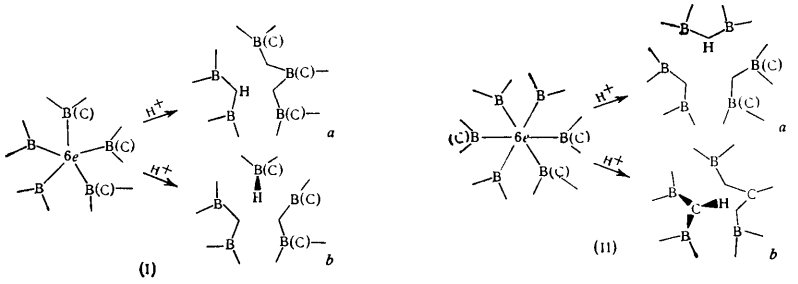


Figure 44.

metal atoms, for example cobalt(III) and iron(III), and the consequent stabilisation of various dynamic structures of the dianions. On formation of complexes with transition metals, the given electronic system of the dianion is fixed to a greater or smaller extent and it is possible to isolate complexes having a definite structure.

The structure of the dianions is also fixed on protonation. However, it is not always identical with the structure of the corresponding carborane ligands in transition metal complexes. On interaction of the bonding orbitals in the open face with a proton, the electron pairs are localised. Two versions of such localisation are possible. In the first a system of two two-centre orbitals and a three-centre B—H—B bond is formed as a result of the protonation of the dianion. (The formation of a B—H—C bond and even more so a C—H—C bond in the final structure is unlikely in view of the excess positive charge on the carbon atoms relative to the boron atoms in the open face.) The initial pentagonal or hexagonal face of the dianion is then fixed. In the second version the system of bonding orbitals in the open face is disturbed owing to the localisation of electrons at one of the atoms with formation of a C—H or B—H σ bond. For understandable reasons, the formation of a C—H σ bond is preferable (localisation of an electron pair at the given atom). The carbon atom thus forms two σ bonds with two substituents. The remaining four electrons are accommodated at two two-centre orbitals. In the case of a hexagonal face one may then expect its narrowing, since the four electrons in the two two-centre orbitals cannot bind a system of six atoms (Fig. 44). The protonation of $R_2C_2B_{10}H_{10}^{2-}$, leading to the monoanion $R_2C_2B_{10}H_{11}^{-}$, one of the isomers of which has a structure (Fig. 39) where one of the carbon atoms is linked by σ bonds to R and H and is located above the plane of the open pentagonal face [127,128], may serve as an example.

Scheme Ia in Fig. 44 occurs in the protonation of, for example, the dicarbollide ions $C_2B_9H_{11}^{2-}$ (the fragments of the possible valence structures are indicated in the Figure). The protonation of the dianion with formation of a monoanion having the structure IB is not so far known. Scheme II can describe the protonation of $C_2B_8H_{10}^{2-}$ derived from 1,2-$C_2B_8H_{10}$ (II*a*) and of $C_2B_{10}H_{12}^{2-}$ derived from 1,2-$C_2B_{10}H_{10}R_2$ (II*b*). The II*b* fragment was taken from Tolpin and Lipscomb [127].

Similarly to the formation of dianions (Figs. 42 and 43), one may expect the addition of not only two but also of four and more electrons to carborane molecules with the corresponding structural rearrangements. If one begins with a carborane containing n atoms in the polyhedron, the tetra-anions should give rise to a molecule isoelectronic with *arachno*-carboranes having a structure representing a fragment of a polyhedron with two vertices more than in the initial *closo*-carborane, i.e. $n + 2$, while in the case of hexa-anions the resulting structure should have three vertices more, i.e. $n + 3$, and so on. Indeed, complexes have been obtained with cobalt(III) in which the carborane ligands can be regarded as tetra-anions and hexa-anions: $C_2B_6H_8^{4-}$, $C_2B_8H_{10}^{4-}$, $C_2B_7H_9^{6-}$, etc. [83,88,202]

2. Oxidation of Carboranes

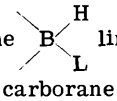
Molecules with the closed structure of the isoelectronic series $B_nH_n^{2-}$, $CB_{n-1}H_n^{-}$, and $C_2B_{n-2}H$ can not only combine with two electrons, but theoretically can also give up two electrons. Indeed the system of bonding orbitals in the skeleton of these molecules includes three two-centre and $n - 2$ three-centre bonds, which follows from the solution of the equations †

$$2x + 2y = 2n + 2 \text{ (electron balance)},$$
$$3n = 2x + 3y \text{ (orbital balance)},$$
$$x = 3,\ y = n - 2,$$

where n is the number of atoms in the polyhedron, x the number of two-centre orbitals, and y the number of three-centre orbitals. After the removal of two electrons, three two-centre bonds can rearrange to two three-centre bonds with retention of the structure as a whole or, if possible, with increase of molecular symmetry. Thus, in principle, it is possible to obtain, for example, the species $C_2B_nH_{n+2}^{2+}$ or the corresponding derivatives $C_2B_nH_{n+1}^{+}$ and $C_2B_nH_n^{0}$—their deprotonation products. Isoelectronic analogues of such systems are known in the series of boron hydrides, for example B_4Cl_4 (tetrahedron), [203-205] B_8Cl_8 (dodecahedron), [206-209] and B_9Cl_9H. [210] The last two compounds are isoelectronic with $C_2B_6H_8^{2+}$ and $C_2B_7H_9^{2+}$ respectively.

The oxidation of the dianions to neutral *closo*-carboranes can be treated formally as a process which is the reverse of the addition of electrons (Figs. 42 and 43) and which leads to the closure of the open structure of the dianion. The oxidant interacts with the bonding two-electron five- or six-centre orbitals, but, in contrast to the usual electrophilic agents, does not fix the possible structures of the dianion, forming a bond with the carborane ligand and resulting in the closure of the *nido*-structure and to a *closo*-structure as a result of electron transfer from the dianion [211]. The formation of particular isomers of *closo*-carboranes may be determined both by the existence of dynamic structures and, mainly, by the mode of closure of the pentagonal and hexagonal faces of the dianions, i.e. by the energy of the transition state whose structure is probably close to that of the dianion—oxidant transition complex.

3. Reactions of Carboranes with Nucleophilic Agents

The mechanism of the interaction of carboranes with nucleophilic agents resembles in the first stage the interaction with an electron pair. The nucleophilic agent interacts with a three-centre orbital, with formation of a two-centre orbital and a boron—nucleophilic agent σ bond (Fig. 45). As a result, the *closo*-structure opens at the site of attack by the nucleophilic agent, as in electron addition, and an open face is formed. Depending on the nature of the carborane and the attacking nucleophilic species, the  linkage may be retained in the residual part of the carborane molecule, or the boron atom may be eliminated after the addition of a second molecule of the nucleophilic agent. For example, the reaction of 1,6-$C_2B_4H_6$ with Me_3N leads to the opening of the *closo*-carborane molecule [73]. The sequence of the electronic and structural rearrangements of the molecule in this reaction

† This set of equations is a special case of the set of Lipscomb's equations put forward to describe boron hydrides and other compounds in terms of the topological theory [4].

can be represented by the scheme in Fig. 46. The electron pair of the nitrogen atom interacts with the three-centre $C_{(1)}-B_{(2)}-B_{(3)}$ orbital to form the $Me_3N-B_{(2)}$ σ bond. The $B_{(2)}-H$, $B_{(2)}-B_{(5)}$, and $B_{(4)}-B_{(5)}-B_{(6)}$ bond orbitals then rearrange in such a way that the molecule is opened still more, and a pentagonal pyramid is formed, the hydrogen atom linked by a σ bond to the $B_{(2)}$ atom migrating to the bridge position.

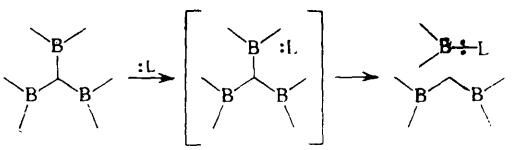


Figure 45.

Another example is provided by the reaction of $C_2B_9H_{11}$ with Lewis bases. The nucleophilic agent L interacts with a three-centre orbital, for example between the $B_{(1)}$, $C_{(3)}$, and $B_{(6)}$ atoms, as a result of which a $B_{(6)}-L$ σ bond is formed and the structure opens. The hydrogen atom linked to $B_{(6)}$ in the initial carborane moves to the bridge position in the product (Fig. 47). According to this scheme, the formation of the 3-isomer for certain L as a result of the opening of the $C_2B_9H_{11}$ structure on the side of the attacking L species [112] is unlikely. The 10-L-7,9-$C_2B_9H_{11}$ isomer is probably formed initially and is converted into 3-L-7,9-$C_2B_9H_{11}$ as a result of the migration of the $B_{(8)}$ atom.

The cleavage of 1,2-(1,7)-$C_2B_{10}H_{12}$ with alkali [119] is illustrated by the scheme in Fig. 48. The mechanisms of the cleavage of $R_2C_2B_{10}H_{10}$ by other nucleophilic agents, such as BuLi, RMgX, piperidine, etc., are similar [212-214]. The intermediate $C_2B_{10}H_{12}R^-$ is an electronic analogue of the dicarbadodecaborate monoanion $C_2B_{10}H_{13}^-$ formed on protonation of the dianion $C_2B_{10}H_{12}^{2-}$. The mechanism of the formation of $C_2B_7H_{13}$ in the cleavage of 1,6-$C_2B_8H_{10}$ with alkali can be represented similarly [100]. Apart from the addition of OH and the elimination of a boron atom, there is in this case a reduction stage, i.e. the transfer of two electrons to the molecule with formation of an *arachno*-carborane.

The general characteristics of the interaction of nucleophilic agents with a three-centre bond are probably manifested not only for *closo*-carboranes but also for *nido*-carboranes having an open B–H–B three-centre bond. Naturally reactions involving the closed B–B–B bonds of the nucleus are also possible. The reactions involving B–H–B bonds must begin, like the reactions involving the three-centre B–B–B bond, with the supply of electrons to the energetically lowest unfilled B–H–B orbital and a subsequent rearrangement of the resulting system via schemes I and II (Fig. 49). Reactions such as the addition of electrons to diborane with formation of $B_2H_6^{2-}$ [215] and the elimination of the bridge hydrogen atom from *nido*-carboranes and boron hydrides by bases or alkali metals proceed similarly. The reactions of carboranes with open three-centre B–C–B bonds (for example, 1,2-$C_2B_4H_6$) [50] can be described by similar schemes. As in reactions involving a closed three-centre bond, in this case the interaction with nucleophilic agents (or electron addition) must evidently be accompanied by the opening of the carborane molecule and the ligand must apparently form a bond with a boron atom. Subsequently, in the interaction with a second ligand molecule, the boron atom may be eliminated.

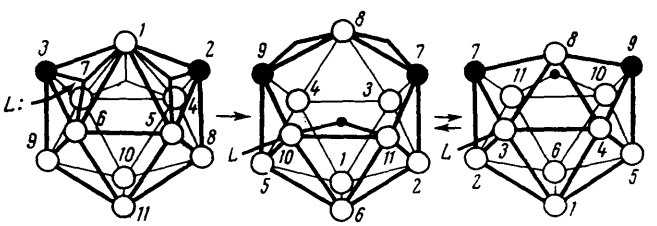


Figure 47.

4. Reactions of Carboranes with Electrophilic Agents

In considering the reactions of carboranes with electrophilic agents, it is logical to treat them as reactions involving two-centre bonds. Indeed there are atoms in carboranes with free electrons, i.e. not involved in the formation of a bond, and the vacant orbital of the electrophilic agent E (which is present or formed in the course of the reaction) interacts with a bonding two-centre orbital (possibly with an antibonding orbital in the transition state, as suggested, for example, by Nefedov et al. [216]); this

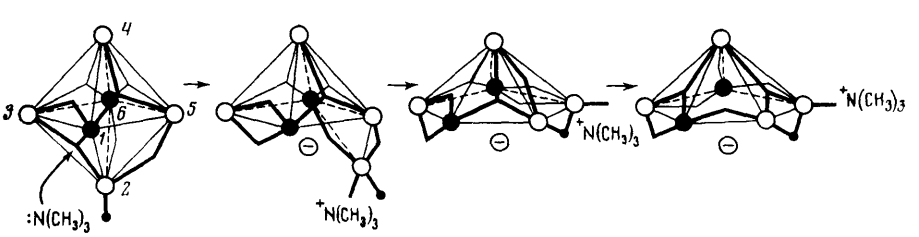


Figure 46.

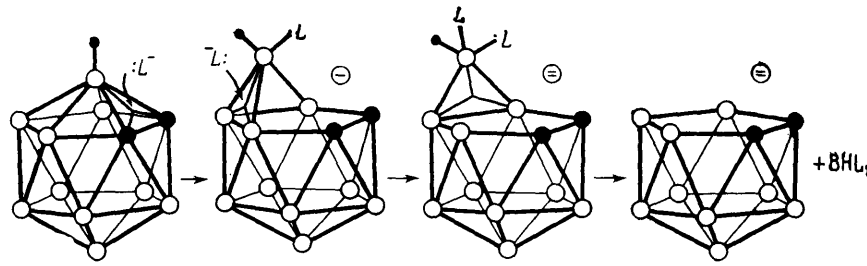


Figure 48.

involves the formation of a three-centre orbital. The possible versions of the three-centre bond formed are presented in Fig. 50 (I)‡.

The nature of the intermediate complex of the carborane with the electrophilic agent and the type of the three-centre bond formed depend on the distribution of electron density among the bonds, the bond polarisabilities, and the characteristics of E, i.e. ultimately on the energy of the orbitals of the reactants and the transition state. On formation of a three-centre bond, the reaction can proceed in several ways.

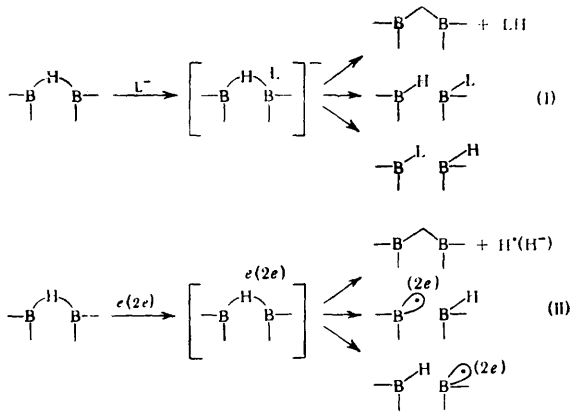


Figure 49.

1. The removal of a proton (H^+) and the formation of substitution products, as, for example, in Fig. 50 (II). The possibility of the formation of isomeric substitution products follows from this scheme. Indeed, depending on the reaction conditions and the nature of the catalyst, the ratio of the isomers formed in the halogenation of carborane(12) varies [217]. In many cases electrophilic substitution leads to a unique product, for example alkylation and halogenation of $4,5\text{-}C_2B_7H_9$ lead to $6\text{-}E\text{-}4,5\text{-}C_2B_7H_9$ (E = Me, Et, or Br). [92] In the series of boron hydrides protonation of $B_{10}H_{10}^{2-}$ leads to the formation of $B_{10}H_{12}$ containing three-centre B–H–B bonds involving the boron atoms at the vertices, which in an acid medium take part in the isotope exchange of hydrogen atoms for deuterium atoms [38]. Deuterium exchange involving $1,2\text{-}C_2B_{10}H_{12}$ in an acid medium leads to the substitution of the hydrogen atoms at all the boron atoms [218].

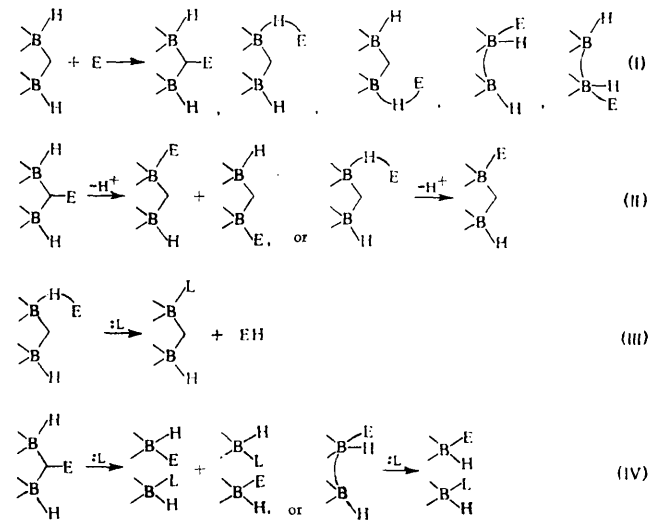


Figure 50.

2. The rupture of a three-centre B–H–E bond, possibly under the influence of the nucleophilic agent (see the interaction of three-centre bonds with nucleophilic agents), with formation of an E–H bond and a vacant orbital at the B atom, which interacts rapidly with an electron donor (when a nucleophilic agent is involved in the process, simultaneously with formation of an E–H bond), as shown, for example, in Fig. 50 (III). The oxidative hydroxylation of carboranes formally proceeds via a similar mechanism [110,121].

3. The rupture of a three-centre B–B–E bond. This stage can also be initiated by the nucleophilic agent [Fig. 50 (IV)]. The *closo*-structure is then of course opened

‡ The generally accepted notation for three-centre bonds is used. For bonds of the open type, such representation can be inconsistent in certain cases with the geometrical structure, i.e. in the transition state the B–H–E bond may prove to be linear.

with formation of B–E and B–L bonds. The opening of the $B_{10}H_{12}^{2-}$ structure in the series of boron hydrides takes place in this way in the interaction with Et_2S in an acid medium, resulting in the formation of $B_{10}H_{12}(SEt_2)_2$.[219] The reaction of 1,6-$C_2B_8H_{10}$ with hydrochloric acid does not stop at any intermediate stage and the opening is accompanied by the breakdown of the structure; boric acid is formed[100]. The breakdown of carboranes in an acid medium in the presence of a palladium catalyst and the oxidative degradation of carboranes, for example of 2,3-$C_2B_9H_{11}$ to $C_2B_7H_{13}$ [32] or of 7,8-$C_2B_9H_{12}^-$ to 5,6-$C_2B_8H_{12}$,[95] can probably be included among reactions of this type.

---o0o---

In conclusion we must note that there may be an alternative to the proposed reaction mechanisms, i.e. in principle, nucleophilic reactions, including the addition of electrons to two-centre bonds and electrophilic reactions involving three-centre bonds, can proceed via the following mechanisms.

1. As already mentioned, the interaction with nucleophilic agents begins with the accommodation of electrons in the nearest orbital (the energetically lowest unoccupied orbital), which is a non-bonding or weakly antibonding orbital in a three-centre bond and an antibonding orbital in a two-centre bond (Fig. 51). It is easily seen that in the general case the reaction involving a three-centre bond is energetically preferable ($E^0_{ABC} < E^*_{AB}$). However, in many cases the two-centre bond is weak, i.e. the energy of the bonding orbital is enhanced and that of the antibonding orbital is reduced. For example, electrons add to *C*-halogenocarboranes(12) at the C–halogen bond with formation of a halide ion and $\geq C^-$: after hydrolysis, the unsubstituted carborane is formed[201]. The reaction of *B*-halogenocarboranes involves both the boron–halogen bond and the three-centre bonds in the nucleus. The former process leads to unsubstituted carboranes and the latter to the dianion of the halogenocarborane, the oxidation of which leads to a mixture of the possible isomers of the halogenocarborane[201].

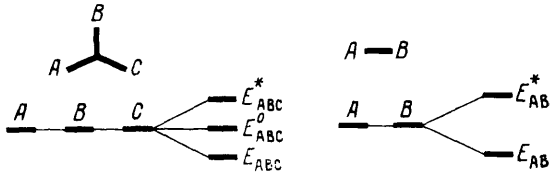


Figure 51.

2. The reactions of electrophilic agents via three-centre bonds can be, in principle, represented by the scheme in Fig. 52:[220,221] the carborane structure is opened with formation of a vacant orbital at one of the atoms, this being followed by rapid interaction of the latter with the nucleophilic agent and the formation of a B–E bond. We believe this mechanism to be unlikely, although it can account for certain reactions, for example the degradation of the carborane nucleus.

Comparison of the foregoing considerations with data from other chemical fields suggests that the interactions of electrophilic agents with two-centre bonds, particularly σ bonds, with formation of three-centre bonds are of a general type. For example, electrophilic reactions of compounds containing an "electron-deficient" atom (B, Be, Al, Ga, etc.), carbenes, and other similar compounds or 'onium compounds, including carbonium ions, proceed in this way. For example, Olah and coworkers have been successfully developing the concept of the intermediate formation of three-centre C–E–C and C–E–H bonds in organic chemistry (here E = R^+, NO_2^+, H^+, etc.).[222–228]

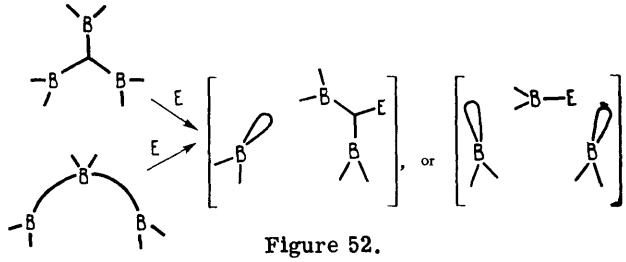


Figure 52.

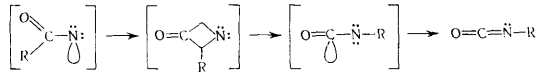
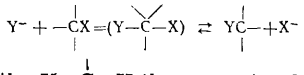


Figure 53.

The concept of the intermediate formation of three-centre bonds can be used successfully in describing certain intermediate stages in electrophilic substitution reactions of aromatic compounds. Such bonds are undoubtedly formed in many rearrangements involving a carbonium ion or an atom with a vacant atomic orbital (sextet rearrangements) (Fig. 53). Thus, three-centre bonds, which are so characteristic of "electron-deficient" compounds (Group III elements) are characteristic also of compounds formed by Group IV–VII elements. This applies in the first place to the intermediates and transition states in such reactions when the element can form a vacant orbital. We may note that three-centre bonds have been successfully invoked to described many inert gas compounds. For example, in the linear XeF_2 molecule the atoms are joined by a three-centre bond of the open type: Xe (the central atom) supplies the 5*p* orbital containing an electron pair and the two fluorine atoms each provide a 2*p* orbital containing one electron. The four electrons are accommodated in the bonding and non-bonding orbitals. All synchronous reactions involving three (and more) centres probably also proceed via an intermediate state in which three-centre (and many-centre) orbitals are formed. For example, in the S_N2 reactions



the formation of the Y–C–X three-centre bond may be expected in the transition state, two electrons being accommodated in the bonding orbital and two in the non-bonding three-centre orbital.

We believe that consideration of the reactions of carboranes, boron hydrides, and related compounds with nucleophilic and electrophilic agents in the light of ideas concerning three-centre and two-centre bonds permits a prediction of the possible modes of the reactions and leads to a better understanding of their mechanisms.

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The Stereochemistry of Optically Active Thio-derivatives of Phosphorus-based Acids

M.Mikołajczyk and M.Leitloff

The review deals with the literature on the separation of chiral thio- and seleno-derivatives of phosphorus-based acids into optical isomers and their most important stereospecific transformations are discussed. Particular attention is concentrated on the analysis of the configurational relations between chemical and physicochemical methods for the determination of the absolute configurations of optically active thio-derivatives of phosphorus-based acids.
The bibliography includes 121 references.

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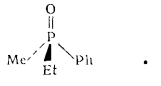
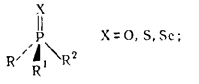
I. INTRODUCTION

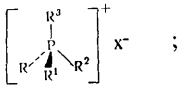
The stereochemistry of organic compounds containing a heteroatom in the molecule as the centre of asymmetry began to develop at the beginning of the present century. At the same time the first attempts were made to resolve chiral organophosphorus compounds into optical isomers. In 1911 Meisenheimer and Lichtenstadt[1] obtained the optically active ethylmethylphenylphosphine oxide and demonstrated for the first time the steric configuration of tetracoordinate phosphorus derivatives:



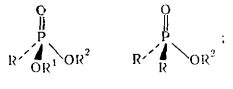
Although subsequently many investigators attempted to resolve chiral organophosphorus compounds, in the course of several decades these were successful in only a few cases. The failure of the majority of the experiments was due to the difficulties associated with the selection of the appropriate resolving agent, forming crystalline diastereoisomers with the test compounds. It was not until the 1950s that much progress was achieved in this field. Many phosphorus compounds which have been resolved into optical isomers are now known. They can be combined into at least six main classes, namely:
(a) phosphine oxides, sulphides, and selenides[2-4]:



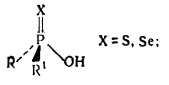
(b) quaternary phosphonium salts[5,6]:



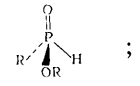
(c) esters of phosphonic and phosphinic acids[7]:



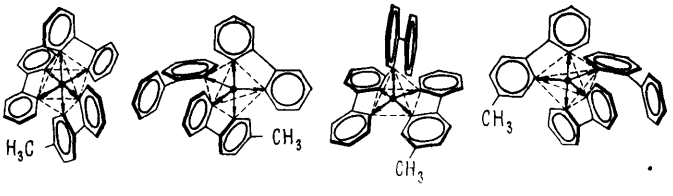
(d) thio- and seleno-derivatives of phosphorus-based acids:



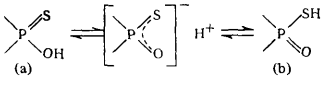
(e) phosphinates[8-20]:



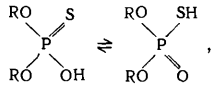
(f) compounds of pentacovalent and hexacovalent phosphorus[21]:



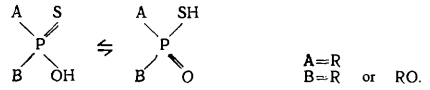
The recent considerable progress in research on the stereochemistry of phosphorus has been reflected in many reviews[6,22-29]. Together with optically active phosphine oxides and quaternary phosphonium salts, monothio-derivatives of phosphorus-based acids are of greatest importance for the development of the stereochemistry of organophosphorus compounds. The special role of these compounds in phosphorus chemistry is a consequence of their high reactivity and interesting chemical structure. In contrast to the oxygen-containing phosphorus-based acids >P(O)OH and the dithio-derivatives of phosphorus-based acids >P(S)SH, the monothio-derivatives can exist in two tautomeric forms: thionic (a) and thiolic (b):



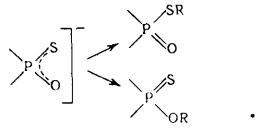
The tautomeric equilibrium between these compounds has been investigated in detail by Kabachnik et al.[30], who showed that both tautomeric forms of dialkylphosphorothioic acids are involved in the equilibrium in comparable amounts:



while in the case of phosphonothioic and phosphinothioic acids the equilibrium is almost completely displaced towards the thionic form:



The monothioacids have ambident anions[31, 32] which can react in two ways with electrophilic agents with the consequent formation of two types of derivatives: thiolo- and thiono-:



The reactivity of the anion can be satisfactorily accounted for with the aid of Pearson's concept[33,34] of "hard" and "soft" acids and bases. The "hard" basic centre of the anion is the more electronegative oxygen atom, which reacts more readily with "hard" acid centres, such as the phosphoryl or thiophosphoryl phosphorus atom, the silicon atom in silyl halides, the carbon atom in the carbonyl group, etc. On the other hand, the sulphur atom in the anion of the thioacid, which is a "soft" base, reacts more readily with "soft" electrophilic agents such as the sp^3-hybridised carbon atom in alkyl halides or halogen cations.

After the publication of the first successful experiments on the resolution of chiral thio-derivatives of phosphorus-based acids into optical isomers, the rapid development of the search for new easy methods of synthesising other representatives of compounds of this class began. At the same time research was started on the stereochemistry of the reactions of optically active thio-derivatives of phosphorus-based acids, the main aim of which was to investigate the stereochemistry of nucleophilic substitution at the asymmetric phosphoryl and thiophosphoryl centres. The studies by Aaron in the USA, Hudson in England, and Michalski and Ratajczak and Mikolajczyk in Poland have been of great importance in the development of the dynamic stereochemistry of thio-derivatives of phosphorus-based acids.

In studies on the stereochemistry of phosphorus much attention has been devoted recently to the problem of the absolute configuration of the optically active thioacids in connection with their exceptionally important position in the numerous family of chiral phosphorus compounds and the great biological activity of some of their derivatives (particularly thiolate esters and acid fluorides). Vigorous research during the last five–six years led to the determination of the absolute configurations of almost all the known optically active thioacids and to the development of many convenient chemical and physicochemical methods for the determination of the chirality of the phosphorus atom in the thioacids.

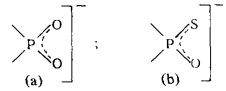
The above considerations led the present authors to write this review of research on the stereochemistry of thio-derivatives of phosphorus-based acids, which constitutes the first survey of the results of studies on the absolute configurations of the chiral acids together with a description of data concerning methods for their resolution into optical isomers and the analysis of their stereospecific transformations.

II. METHODS FOR THE SEPARATION OF CHIRAL PHOSPHORUS-BASED THIOACIDS INTO OPTICAL ISOMERS

The first attempts at the separation of phosphorus-based acids into optical isomers were undertaken as early as 70 years ago. However, initially attention was concentrated mainly on unsuccessful attempts to resolve oxygen-containing phosphorus-based acids:

The names of Caven[35], Kipping[36], Pope[37], Gibson[37], Ephraim[38], Arbuzov[39], and many other investigators are associated with research in this field.

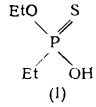
The study by Ephraim (1911), who demonstrated that oxygen-containing phosphorus-based acids cannot be separated into optical isomers since their anions (a) are symmetrical, merits special attention:



Ephraim was the first to draw attention to the fact that the substitution of one of the oxygen atoms by a sulphur atom leads to the formation of an asymmetric anion (b) and his further research was concerned with the resolution of chiral monothio-derivatives of phosphorus-based acids. However, his first attempt at the resolution of phosphoramidothioic acid,

was unsuccessful, since this acid did not form crystalline diastereoisomeric salts with the alkaloids which he had chosen. The later attempts by Arbuzov and Kamai[39] to resolve chiral thio-derivatives of phosphorus-based acids were likewise unsuccessful for the same reason.

It was not until 1956 that Aaron and Miller[40,41] succeeded for the first time in separating a chiral thioacid of phosphorus into enantiomers. This was *O*-ethyl ethylphosphonothioic acid (I), which was separated into optical isomers with the aid of the alkaloids quinine and brucine:



A somewhat simplified process for the preparation of this acid was described later by Michalski and Ratajczak[42].

In recent years Aaron and coworkers[43] resolved a series of *O*-alkyl alkylphosphonothioic acids (II–VI) by the fractional crystallisation of their diastereoisomeric salts with quinine:

(II) R=Me, R^1=Me; (V) R=Et, R^1=Me;
(III) R=Me, R^1=Et; (VI) R=i-Pr, R^1=Et.
(IV) R=Me, R^1=i-Pr;

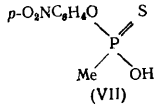
The characteristics of the optical isomers which they obtained are given in Table 1.

Table 1. Characteristics of the optical isomers of *O*-alkyl alkylphosphonothioic acids $(R^1O)R^2P(S)OH$.

№	R^1	R^2	Resolving amine	Dicyclohexylammonium salt			References
				m.p., °C	(+)$[\alpha]_D$,°	(-)$[\alpha]_D$,°	
I	C_2H_5	C_2H_5	quinine	160	6.94 (13.205)[a]	7.11 (13.6)[a]	41
II	CH_3	CH_3	a) quinine b) α-phenyl ethylamine	180	6.6 6.37	2.3 6.35	43 45
III	C_2H_5	CH_3	a) quinine b) α-phenyl ethylamine	127	7.0 (9.6)[a] 8.47	4.2 8.47	43 45
IV	i-C_3H_7	CH_3	a) quinine b) α-phenyl ethylamine	126	7.6(13.6)[a] 7.76	7.6(13.9)[a] 7.72	43 45
V	CH_3	C_2H_5	quinine	185	4.1	7.0	43
VI	C_2H_5	i-C_3H_7	quinine	149	6.5	7.0	43
VII	p-$NO_2C_6H_4$	CH_3	—	—	—	—	44
VIII	n-C_4H_9	CH_3	α-phenyl ethylamine	116	7.25	7.21	45
IX	CH_3	t-C_4H_9	α-phenyl ethylamine	—	13.18[a]	10.5[a]	46
X	CH_3	i-C_3H_7	α-phenyl ethylamine	180	4.6	4.2	47
XI	n-C_3H_7	CH_3	α-phenyl ethylamine	—	1.3[a]	1.06[a]	48

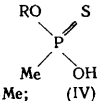
[a] Free acid.

In 1963 Boter and Ooms[44] separated *O*-p-nitrophenylmethylphosphonothioic acid (VII) into optical isomers:



(VII)

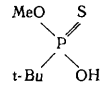
In his search for a simple method of synthesising optically active Sarin, one of the most important inhibitors of cholinesterase, Boter[45] developed in 1967 a new method for the separation of chiral *O*-alkyl methylphosphonothioic acids (II–IV, VIII):



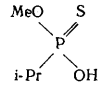
(II) R=Me; (IV) R=i-Pr;
(III) R=Et; (VIII) R=n-Bu.

He used optically active α-phenylethylamine (both optical isomers) as the resolving agent. The first stage in the resolution consisted in the introduction of half a mole of the dextrorotatory amine into an etheral solution of one mole of the racemic acid and the separation of the rapidly crystallised salt of the (+)-amine with the (+)-thioacid. In the second stage the acid remaining in solution was treated with an equimolar amount of the laevorotatory amine and the diastereoisomeric salt of the latter with the laevorotatory acid was isolated.

α-Phenylethylamine is nowadays finding extensive application in the separation of chiral thio-derivatives of phosphorus acids in view of its ability to form readily crystallisable salts and because of the ready availability of both its enantiomers. The resolution by this amine of *O*-methyl t-butylphosphonothioic acid (IX) by Krawiecka and Michalski[46] and of *O*-methyl isopropylphosphonothioic acid (X) by Mikołajczyk and Omelańczuk[47] can serve as examples:



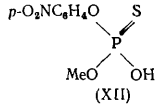
(IX)



(X)

Leitloff[48] attempted to separate *O*-propyl methylphosphonothioic acid (XI) into optical isomers with the aid of α-phenylethylamine by Boter's method. However, the inadequate optical purity of the enantiomers obtained by this method shows that the latter must be modified for this acid.

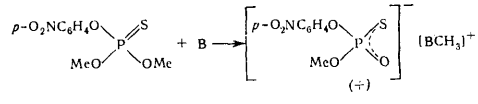
One year after the publication of Aaron's first communication concerning the separation of the optical isomers of *O*-ethyl ethylphosphonothioic acid (I) Hilgetag and Lehman[49] described a method for the separation of *O*-methyl *O*-*p*-nitrophenyl phosphorothioic acid (XII):



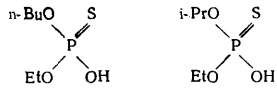
(XII)

OO-Dimethyl *O*-*p*-nitrophenyl phosphorothionate was converted by this method into the silver salt of the acid (XII) as a result of dealkylation with silver nitrate; the salt was then treated with methylstrychnine iodide. The diastereoisomeric methylstrychnine salts with the rotations $[\alpha]_D = -12.4°$ and $[\alpha]_D = +9.7°$ were separated by fractional crystallisation. In an acid medium both salts give rise to unstable optically active isomers of the acid (XII), which were converted into lead salts with the rotations $[\alpha]_D = -17.4°$ and $[\alpha]_D = +18.9°$ respectively. The optical isomers of the acid (XII) were the first examples of optically active phosphorus-based thioacids.

The same workers[50] also developed a new interesting method for the separation of the isomers of the acid (XII), which is in the nature of partial asymmetric synthesis. It consists in the asymmetric demethylation of *OO*-dimethyl *O*-*p*-nitrophenyl phosphorothionate by strychnine. The dextrorotatory salt of the thioacid with $[\alpha]_D = +13.8°$ (60–80%) predominated in the mixture of the diastereoisomeric methylstrychnine salts of the acid (XII):



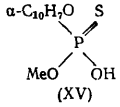
The next examples of optically active phosphorothioic acids are *O*-butyl *O*-ethyl phosphorothioic acid (XIII) and *O*-ethyl *O*-isopropyl phosphorothioic acid (XIV), which were separated into their isomers by Michalski et al.[51]



(XIII) (XIV)

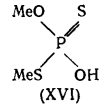
These thioacids were resolved with the aid of cinchonidine and quinine. Although the optical rotations of the resulting enantiomers of both thioacids were too low to be measured (on apparatus with a sodium source), nevertheless their derivatives were optically active, which demonstrated their partial separation.

In 1968 yet another chiral phosphoromonothioic acid was resolved, namely *O*-methyl *O*-α-naphthyl phosphorothioic acid (XV). Donninger and Hutson[52] achieved this by the fractional crystallisation of the diastereoisomeric salts of (XV) with the aid of (+)- and (−)-ephedrine:



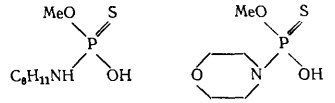
(XV)

In the following year Teichmann[53] resolved the dimethyl ester of phosphorothiolothionic acid (XVI), which contains two sulphur atoms in the molecule. The resolution was achieved by the asymmetric demethylation of *OOS*-trimethyl phosphorothiolothionate with strychnine:



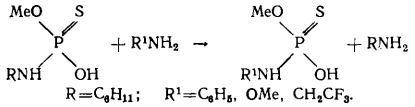
(XVI)

The optically active phosphoromidothioic acids obtained by Hamer[54] constitute a separate group. In 1965 Hamer resolved *N*-cyclohexyl *O*-methyl phosphoramidothioic acid (XVII) by the fractional crystallisation of its diastereoisomeric quinine salts:



(XVII) (XVIII)

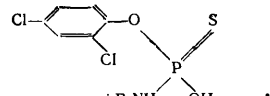
Then, by substituting the amino-residue, he obtained a whole series of optically active phosphoramidothioic acids:



R=C_6H_{11}; R^1=C_6H_5, OMe, CH_2CF_3.

Several years later Gerrard and Hamer[55] resolved by the same method *O*-methyl phosphoromorpholidothioic acid (XVIII) and isolated its dextrorotatory isomer in the form of the ammonium salt.

The methylammonium salts of both optically active forms of *O*-2,4-dichlorophenyl *N*-isopropyl phosphoramidothioic acid (XIX) were obtained in 1969 by Seiber and Tolkmith[56]. The methylammonium salt of the racemic acid (XIX), synthesised by the demethylation of the corresponding *O*-methyl phosphoramidothioate, was converted into a mixture of diastereoisomeric salts with quinine using quinine sulphate. The diastereoisomers were separated by fractional crystallisation and then, as a result of the substitution of quinine by methylamine, the enantiomeric (+)- and (−)-salts were obtained from them with the rotations $[\alpha]_D = +15.9°$ and $-23.4°$ respectively:



(XIX)

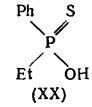
Certain physicochemical properties of optically active phosphorothioic, phosphonothioic, and phosphoramidothioic acids are listed in Table 2.

Table 2. Optically active phosphorothioic, phosphonothioic, and phosphoramidothioic acids $(R^1)R^2P(S)OH$.

№	R^1	R^2	Resolving amine	(+)$[\alpha]_D$,°	(−)$[\alpha]_D$,°	References
XII	*p*-$O_2NC_6H_4O$	CH_3	strychnine	18.9[a] 13.8[d]	17.4[a] 13.1[d]	49 50
XIII	n-C_4H_9O	C_2H_5O	cinchonidine	1.0[b]	1.3[b]	51
XIV	i-C_3H_7O	C_2H_5O	quinine	2.1[b]	2.0[b]	51
XV	α-$C_{10}H_7O$	CH_3O	ephedrine	33.0[e] 53.4[b]	45.9[e] 51.0[b]	52
XVI	CH_3S	CH_3O	strychnine	27.1[c] 14.1[d]	27.9[c] 14.5[d]	53
XVII	CH_3O	$C_6H_{11}NH$	quinine	38.0[c]	37.0[c]	54
XVIII	CH_3O	C_4H_8NO	quinine	2.9[f]	—	55
XIX	2,4-$Cl_2C_6H_3O$	*i*-PrNH	quinine	15.9[f]	23.4[f]	56

[a] Lead salt; [b] *S*-methyl ester; [c] free acid; [d] methylstrychnine salts; [e] ephedrine salt; [f] ammonium salt.

The first example of the series of phosphinothioic acids resolved into optical isomers was ethylphenylphosphinothioic acid (XX). Its partial resolution was achieved by Green and Hudson[57] in 1963 with the aid of quinine as the optically active resolving agent:



(XX)

Several years later other chiral phosphinothioic acids were resolved: methylphenylphosphinothioic acid (XXI), resolved in 1968 by Benschop's group[58], and t-butylphenylphosphinothioic (XXII), resolved in 1971 by Trippet and coworkers[59]. In both cases quinine was used as the resolving agent:

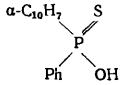
(XXI) (XXII)

The results of studies on ethylmethylphosphinothioic acid (XXIII), partially resolved by Ratajczak, were published in the proceedings of the International Colloquium on Organic Chemistry held in Paris in 1969:[60]

(XXIII)

However, no information about the method used to resolve this acid was published.

Recently Chauzov and Lutsenko[61] resolved α-naphthylphenylphosphinothioic acid (XXIV) by the fractional crystallisation of its diastereoisomeric salts with quinine:



(XXIV)

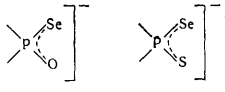
The characteristics of the optical isomers of this acid and other phosphinothioic acids are given in Table 3.

Table 3. Optically active phosphinothioic acids $R^1R^2P(S)OH$.

№	R^1	R^2	Resolving amine	(+) $[\alpha]_D$, °	(−) $[\alpha]_D$, °	References
XX	C_2H_5	C_6H_5	quinine	6.5[a]	6.5[a]	57
XXI	CH_3	C_6H_5	quinine	9.25[a]	9.22[a]	58
XXII	t-C_4H_9	C_6H_5	quinine	21.4[b]	21.4[b]	59
XXIII	CH_3	C_2H_5	—	—	—	60
XXIV	α-$C_{10}H_7$	C_6H_5	quinine	63.8[a] 112.0[b]	64.6[a] 113.0[b]	61

[a] Dicyclohexylammonium salt; [b] free acid.

An interesting class of chiral organophosphorus compounds consists of selenium-containing phosphorus-based acids and thioacids. The negative charge in the anions of these compounds is distributed between selenium and oxygen and selenium and sulphur atoms respectively:



The first example of optically active selenium-containing phosphorus-based acids was *O*-ethyl ethylphosphonothioselenoic acid (XXV), resolved into optical isomers by Krawiecki et al.[62]:

(XXV)

Recently Krawiecka et al.[63] resolved t-butylphenylphosphinoselenoic acid (XXVI) with the aid of α-phenylethylamine:

(XXVI)

Somewhat later Nuretdinov et al.[64] succeeded in resolving *O*-ethyl ethylphosphonoselenoic acid (XXVII) into optical isomers:

(XXVII)

The alkaloids quinine and brucine were used as the resolving bases. The optical rotations of the selenium-containing acids are listed in Table 4.

Table 4. Optical isomers of phosphoroselenoic acids.

No.	Resolving amine	(+) $[\alpha]_D$, °	(−) $[\alpha]_D$, °	References
XXV	quinine	4.9[a] 2.4[b]	6.7[a] 3.8[b]	62
XXIV	α-phenylethylamine	25.6[a]	30.0[a]	63
XXVII	quinine and brucine	11.36[a]	17.54[a]	64

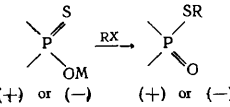
[a] Free acid; [b] dicyclohexylammonium salt.

III. STEREOSPECIFIC REACTIONS OF OPTICALLY ACTIVE PHOSPHORUS-BASED MONOTHIOACIDS

Since optically active monothio-derivatives of phosphorus-based acids have ambident anions, they are very convenient starting materials for the synthesis of thiolo- and thiono-derivatives. Further stereospecific transformations of the compounds obtained directly from the thioacids lead to the synthesis of almost all types of optically active organophosphorus compounds. A detailed description of the many-stage reactions of the thioacids would require the examination of the overall dynamic stereochemistry of phosphorus and would be outside the scope of the present review. We shall therefore consider only those reactions in which the phosphorus-based thioacids are directly involved. The study of the stereochemistry of these reactions greatly assisted in the investigation of the mechanism of nucleophilic substitution at both phosphoryl [P(O)] and thiophosphoryl [P(S)] centres[65].

Optically Active Thiolate Esters

An example of reactions in which the chiral centre is unaffected is provided by the alkylation of the salts of optically active phosphorus-based thioacids, which leads to the formation of optically active thiolate esters:



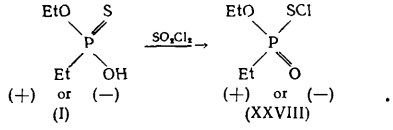
(+) or (−) (+) or (−) (1)

Alkyl halides, and among these alkyl iodides, are usually employed as alkylating agents[66-68]. Dimethyl sulphate is frequently used in the synthesis of methyl thiolate esters[57]. Since none of the bonds involving phosphorus is ruptured in the course of alkylation, the optically active thiolate esters retain the configuration of the initial thioacid.

According to Brewster's asymmetry rule, the sign of the optical rotation of the thiolate esters must be the same as that of the initial thioacids. This has been confirmed in each case described hitherto.

Optically Active Oxophosphoranesulphenyl Chlorides and Diphosphoryl Disulphides

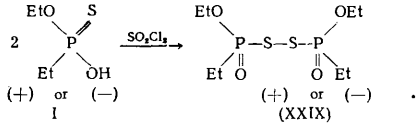
The reactions of phosphorus-based thioacids with chlorine or sulphuryl chloride leads to the formation of optically active oxophosphoranesulphenyl chlorides[42,68]. This was first discovered by Michalski and Ratajczak, who obtained optically active ethoxyethyloxophosphoranesulphenyl chloride (XXVIII) as a result of the chlorination of optically active *C*-ethyl ethylphosphonothioic acid (I):



(2)

As in alkylation, in reaction (2) the bonds involving the chiral phosphorus atom are not ruptured and the configuration of the initial thioacid is retained in the product. Optically active oxophosphoranesulphenyl chlorides are effective starting materials for further syntheses[69].

Optically active diphosphoryl disulphides can also be obtained by the reactions of optically active phosphorus-based monothioacids with sulphuryl chloride[70]. They are formed in the interaction of one molecule of sulphuryl chloride with two molecules of the thioacid:

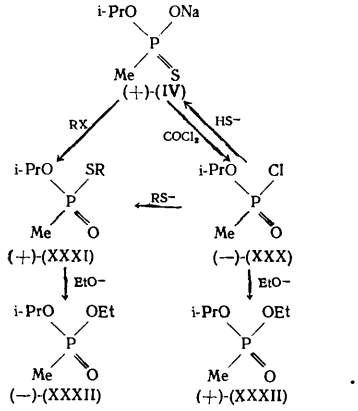


(3)

The disulphide (XXIX) is formed in two stages. Oxophosphoranesulphenyl chloride (XXVIII) is formed in the first stage and in the next stage it reacts with a second molecule of the thioacid. The chiral phosphorus atom is not attacked in either stage and the configuration of the initial acid is retained at both centres of chirality in the disulphide.

Optically Active Phosphoryl and Thiophosphoryl Halides

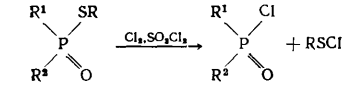
Optically active phosphorus-based monothioacids are the main starting materials for the synthesis of optically active phosphoryl [>P(O)X] and thiophosphoryl [>P(S)X] halides. One of the methods for the preparation of optically active phosphoryl chlorides involves the chlorination of salts of phosphorus-based thioacids with phosgene[66]. Aaron and Miller investigated the stereochemistry of this reaction in connection with the transformation of [−)-*O*-isopropyl methylphosphonochloridate (XXX), obtained by treating (+)-*O*-isopropyl methylphosphonothioic acid (IV) with phosgene:



(4)

The authors concluded that the reaction of the thioacid (IV) with phosgene and the formation of the compound (XXXI) take place with inversion of the configuration at the phosphorus atom.

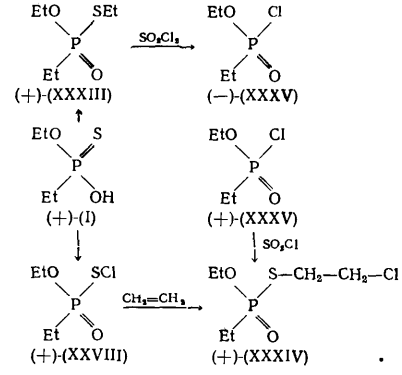
Green and Hudson[71] and independently Michalski and Ratajczak[72] obtained optically active phosphoryl chlorides by chlorinating *S*-alkyl esters of optically active phosphorus-based monothioacids:



(5)

The studies by Green and Hudson showed that chlorination of *S*-alkyl phosphinothioates leads to the formation of the corresponding chlorides with inversion of the configuration at the phosphorus atom.

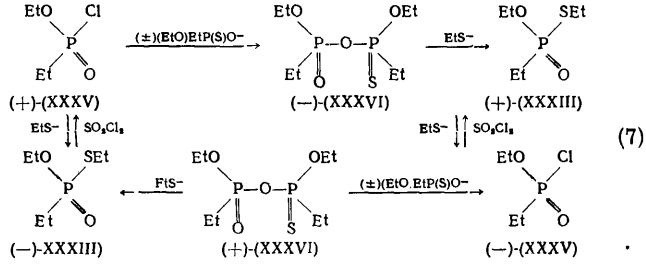
The studies of Michalski and Ratajczak led them to the conclusion that the stereochemistry of the chlorination of phosphonothioates depends on the structure of the substituent R. The mechanism of this reaction has not been elucidated so far. The studies which have been carried out hitherto suggest that the chlorination of the *S*-β-chloroethyl ester proceeds largely with retention of the configuration at the phosphorus atom, while the *S*-ethyl ester is chlorinated with inversion of configuration:



(6)

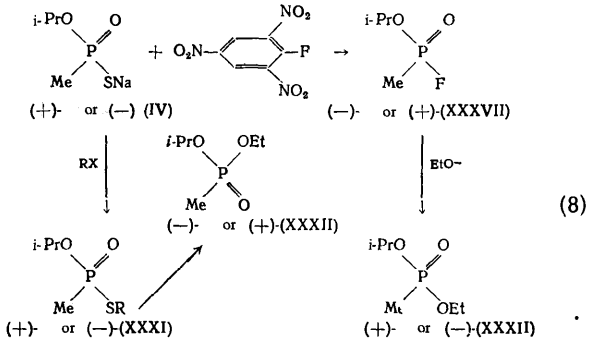
In connection with the stereochemistry of optically active phosphoryl chlorides and thiolate esters, mention should be made of the cyclic process, developed by Ratajczak[73], consisting of six reactions each of which

probably proceeds with inversion of the configuration at the phosphorus atom:



(7)

The reaction of optically active phosphorus-based thioacids with picryl fluoride leads to the formation of optically active phosphoryl fluorides. This reaction was carried out by Boter et al.[74] in the synthesis of optically active Sarin (XXXVII), the well known chlolinesterase inhibitor:



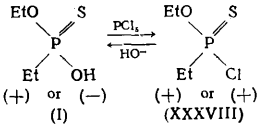
(8)

The sign of the optical rotation of the acid fluoride (XXXVII) obtained in this way is the opposite of that of the initial thioacid. Ethanolysis of the product, which is known to proceed with inversion of the configuration, leads to the formation of the ester (XXXII), which, according to Aaron, has the configuration of the initial acid. On this basis, the authors concluded that the reaction of the thioacid with picryl fluoride takes place with inversion of the configuration at the phosphorus atom.

Although phosphoryl compounds are very interesting, they are not, however, convenient objects for stereochemical studies because of their low optical stabilities†. For this reason, the results obtained can indicate only that the mechanism involving the inversion or retention of the configuration at the phosphorus atom predominates. It was found that the less reactive thiophosphoryl compounds are much more suitable for stereochemical studies.

The difference between the reactivities of phosphoryl and thiophosphoryl compounds is a consequence of the difference between the electron densities at the phosphorus atom in these compounds and the different polarisabilities of the phosphoryl and thiophosphoryl groups[75].

The synthesis by Michalski and Mikołajczak[76-78] of optically active *O*-ethyl ethylphosphonochloridothioate (XXXVIII) was an important achievement in the stereochemistry of thiophosphoryl compounds. This acid chloride is formed in a high yield and with a high optical purity in the reaction of optically active *O*-ethyl ethylphosphonothioic acid (I) with phosphorus pentachloride:

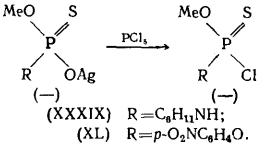


(9)

To determine the mechanism of the chlorination with phosphorus pentachloride, the resulting acid chloride (XXXVIII) was hydrolysed[78], the hydrolysis having been shown previously to involve usually the inversion of the configuration. As a result of the hydrolysis, the authors obtained the initial acid (I). This led them to the conclusion that the chlorination also proceeds with a change of configuration at the phosphorus atom. The high purity and optical activity of the resulting acid chloride (XXXVIII) make the compound a suitable starting material for the synthesis of other optically active organophosphorus compounds and for the investigation of reaction mechanisms[80].

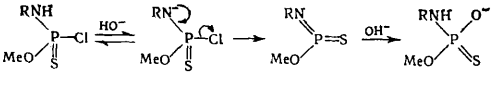
Phosphonochloridothioate derivatives of all optically active *O*-alkyl alkylphosphonothioic acids known at present were obtained similarly[81].

Using the reaction with phosphorus pentachloride, Gerrard and Hamer[82,83] also obtained optically active *O*-methyl *N*-cyclohexyl phosphoramidochloridothionate (XXXIX) and *O*-methyl *p*-nitrophenyl phosphorochloridothionate (XL):



(10)

It is interesting that alkaline hydrolysis of the phosphoramidochloridothionate (XXXIX) leads, in conflict with the above, to the formation of a racemic product, while its solvolysis results in the formation of an optically active product with inversion of the configuration. Under alkaline conditions, the hydrolysis probably proceeds via the following mechanism:



(11)

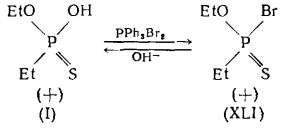
and the racemisation is associated with the formation of an intermediate optically inactive analogue of metaphosphate.

In contrast to the silver salts of optically active phosphorus-based thioacids, their ammonium salts are not convenient starting materials for the synthesis of optically active pure phosphorochloridothionates. Seiber and Tolkmith[56] showed that the reaction of the optically active methylammonium salt of *O*-2,4-dichlorophenyl *N*-isopropyl phosphoramidothioic acid (XIX) with phosphorus pentachloride results in the formation of a partly racemised product (probably via a chlorine–chlorine exchange reaction at the phosphorus atom).

Michalski et al.[84] found that optically active thiophosphonyl bromides can be obtained as a result of the reaction of triphenylphosphine dibromide with optically active

† Optically active phosphoryl halides with high optical stability were obtained recently from phosphorus-based thioacids in which the phosphorus atom is linked to a t-butyl group[63].

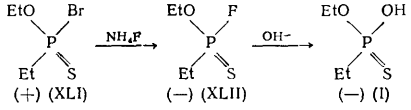
phosphorus-based monothioacids. Optically active *O*-ethyl ethylphosphonobromidothionate (XLI) was obtained by this method:



(12)

Hydrolysis of compound (XLI) leads to the reformation of the initial acid. This proves that the bromination of the thioacid with triphenylphosphine dibromide takes place with inversion of configuration at the phosphorus atom.

It is noteworthy that the optically active phosphonofluoridothionate (XLII) can be obtained from the optically active phosphonobromidothionate (XLI) as a result of the substitution of the bromine atom by a fluorine atom using ammonium fluoride[85]:

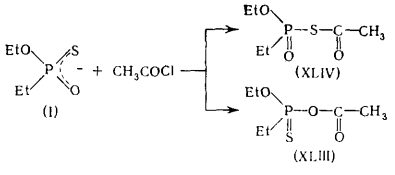


(13)

The result of the hydrolysis of compound (XLII) shows that the halogen exchange reaction is accompanied by the inversion of configuration.

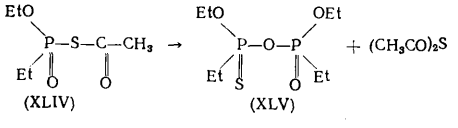
Optically Active *O*-Acyl Phosphonothionates

Omelańczuk and coworkers[86,88] studied compounds of this type and found that *O*-acetyl and *S*-acetyl anhydrides are formed in the reaction of a salt of the optically active *O*-ethyl ethylphosphonothioic acid (I) with acetyl chloride:



(14)

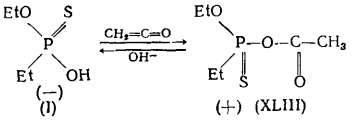
In contrast to the *O*-acetyl anhydride (XLIII), which can be readily isolated, its thiolo-isomer (XLIV) is unstable and "disproportionates" under the reaction conditions with formation of optically active *OO*-diethyl diethylpyrophosphonothioate (XLV) and diacetyl sulphide:



(15)

The ability of the thioacid anion to react in two different ways with acetyl chloride and to form similar decomposition products of the thiol type was observed by Kabachnik and coworkers[87] in the acetylation of diethylphosphinothioate salts.

Mikołajczyk et al.[88] modified the acetylation procedure using the free thioacid instead of its salt and developed a new method for the synthesis of active acetylthiophosphoryl anhydrides in the reaction of optically active phosphorus-based thioacids with keten. They showed that in the acetylation of the free acid with both acetyl chloride and acetic anhydride the amount of disproportionation products of the thiol anhydride (XLIV) diminishes appreciably and the yield of the *O*-acetylanhydride (XLIII) increases. On the other hand, the reaction with keten leads to the exclusive formation of the *O*-acetylation product:

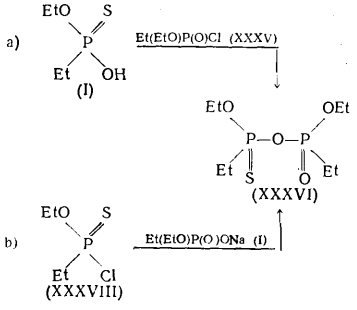


(16)

The configuration of the resulting anhydride (XLIII) corresponds to that of the initial acid, since the centre of chirality is not involved in the reaction. This was confirmed by the hydrolysis of the (+)-isomer of (XLIII) which yielded the initial (−)-acid (I). As expected, in this case the attack by the hydroxy-group is directed to the most electrophilic centre in the molecule, i.e. to the carbonyl group. The configuration of the thioacid residue, which is the group eliminated, does not change.

Optically Active Pyrophosphonothioates and Pyrophosphonodithioates

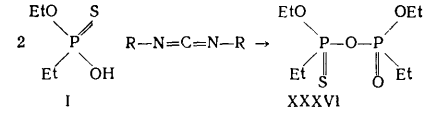
Pyrophosphonomonothioates and pyrophosphonodithioates have been the subject of research by Michalski for several years[89]. The optically active *OO*-diethyl diethylpyrophosphonothionate (XLV) [90] is particularly convenient to investigate because of its ready availability. The starting material for the synthesis is *OO*-ethyl ethylphosphonothioic acid (I) or *O*-ethyl ethylphosphonochloridothioate (XXXVIII) [91] obtained from it:



(17)

Pyrophosphonothioates with one or two optically active centres can be obtained via pathway (a) indicated above. However, in view of the low stability of *O*-ethyl ethylphosphonochloridate (XXXV), the pyrophosphonothioate with two optically active phosphorus atoms obtained in this way has a low optical purity of the phosphoryl centre.

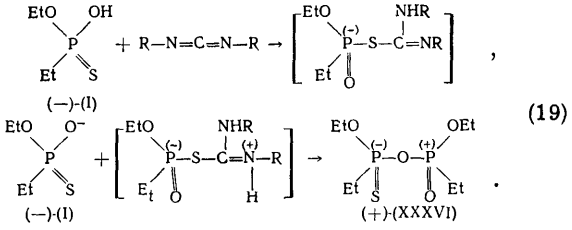
Mikołajczyk[92] developed an interesting method for the synthesis of pyrophosphonothioates with two optically active centres by the reaction of an optically active thioacid with dicyclohexylcarbodiimide:



(18)

OO-Diethyl diethylpyrophosphonothioate (XXXVI) obtained by this method has a high optical purity of the phosphoryl centre. This reaction proceeds in two stages and leads

to the formation of the optically active pyrophosphonothioate (XXXVI) with the opposite configurations at the phosphorus atoms:



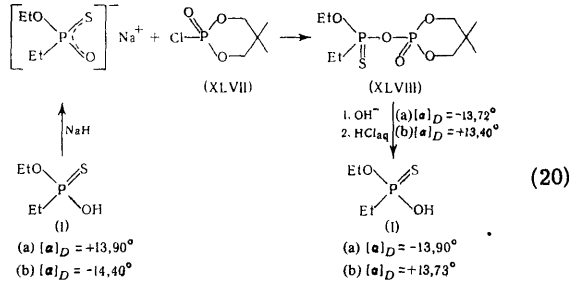
(19)

The relative configurations and the optical purities of both chiral centres in pyrophosphonothioates of this type can be readily determined by cleaving them with nucleophilic agents. The cleavage of compound (XXXVI) is associated exclusively with attack on the phosphoryl centre P(O) and takes place with inversion of the configuration at the attacked phosphorus atom. The thioacid residue is the group eliminated and its configuration is unaltered in the cleavage reaction.

Stereochemical studies on the cleavage of other pyrophosphonothioates showed that nucleophilic attack can be directed also to the thiophosphoryl centre, depending on the type of substituent at the two phosphorus atoms and on the reaction medium.

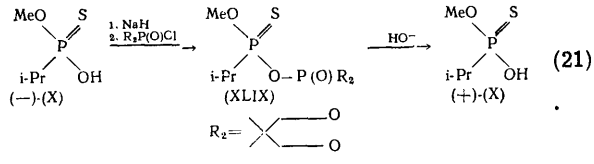
The Walden cycle, developed by Michalski et al.[93], in which the authors employed pyrophosphonothioates (XLVIII) with marked steric hindrance at the phosphoryl centre, merits particular attention in connection with this research.

As a result of two consecutive reactions, condensation of the thioacid (I) with 2-chloro-5,5-dimethyl-2-oxo-1,3-dioxa-2-phosphorinane (XLVII) followed by hydrolysis, one of the enantiomers of *O*-ethyl ethylphosphonothioic acid was converted into its antipode. Since the condensation reaction does not affect the symmetry of the chiral centre, this result proves unambiguously that alkaline hydrolysis proceeds with inversion of configuration at the thiophosphoryl phosphorus atom:



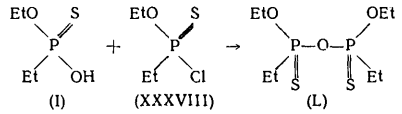
(20)

The Walden cycle was developed for *O*-methyl isopropylphosphonothioic acid (X) in order to demonstrate that nucleophilic substitution in isopropylphosphonothioates proceeds in the same way as in ethylphosphonothioates, i.e. with inversion of the configuration at the phosphorus atom[81]:



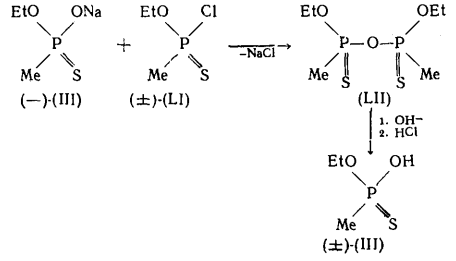
(21)

Pyrophosphonodithioates are formed as a result of the reaction between an optically active thioacid and a phosphonochloridothioate[91,94]:



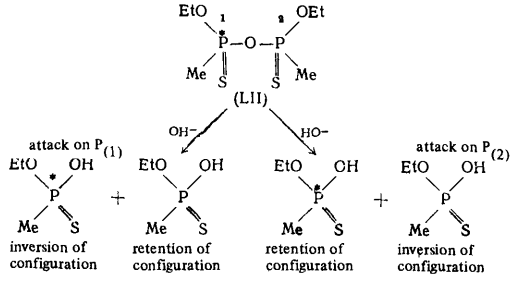
(22)

Using pyrophosphonodithioates, Green and Hudson[94] investigated for the first time nucleophilic substitution at the thiophosphoryl centre and found that it proceeds with inversion of the configuration at the phosphorus atom. They studied the hydrolysis of the optically active *OO*-diethyl dimethylpyrophosphonodithioate (LII), obtained by the reaction of a salt of the optically active acid (III) with (+)-*O*-ethyl methylphosphonochloridothionate (LI):



(23)

They found that the hydrolysis leads to the formation of racemic *O*-ethyl methylphosphonothioic acid (III). There are two equivalent phosphorus atoms in pyrophosphonodithioates. Consequently attack by the nucleophilic agent can be directed with equal probabilities to both thiophosphoryl centres. The formation of the racemic acid (III) as a result of the hydrolysis of the pyrophosphonodithioate (LII) with one optically active centre demonstrates the inversion of the configuration at the phosphorus atom. The interpretation of the results obtained by Green and Hudson may be illustrated by the following scheme:



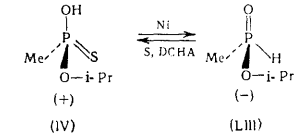
(24)

Further studies on the alcoholysis, mercaptanolysis, and aminolysis of *OO*-diethyl diethylpyrophosphonodithioates[86,88] confirmed that nucleophilic substitution at the thiophosphoryl centre proceeds with inversion of the configuration.

Optically Active Phosphonites

Much attention has been devoted recently to optically active phosphonites:

Reiff and Aaron[12] found that desulphuration of optically active phosphonothioic acids in the presence of nickel as the catalyst is a convenient method for the synthesis of compounds of this type. On heating (*R*)-(+)-*O*-isopropyl methylphosphonothioic acid (IV) in ethanol in the presence of Raney nickel, they obtained the optically active (*S*)-(−)-*O*-isopropyl methylphosphonite (LIII):



(25)

(+) (IV) (−) (LIII)

DCHA = dicyclohexylamine.

The addition of sulphur to the resulting phosphonite in the presence of dicyclohexylamine, which undoubtedly takes place with the retention of the configuration, leads to the reformation of the initial acid. This shows that desulphuration of the acid proceeds without a change in the configuration at the phosphorus atom.

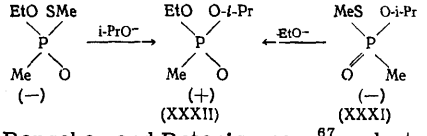
Another method for the synthesis of optically active phosphonites involves their stereospecific inclusion in cyclodextrins[14,18].

IV. DETERMINATION OF THE CONFIGURATIONS OF OPTICALLY ACTIVE PHOSPHORUS-BASED MONOTHIOACIDS BY CHEMICAL CORRELATION‡ AND X-RAY DIFFRACTION

The relative configurations of optically active monothioacids were mentioned for the first time by Aaron et al.[43], who described the resolution of chiral *O*-alkyl alkylphosphonothioic acids (I–VI) into optical isomers. Studies on the biological activities of the corresponding derivatives synthesised from the optically active thioacids showed that the optical isomers obtained from the (−)-thioacids are much more powerful inhibitors of cholinesterases than the enantiomers obtained from the (+)-thioacids. On this basis the authors concluded that the *O*-alkyl alkylphosphonothioic acids (I–VI) with the same sign of optical rotation have the same configuration:

(I) R = Et, R¹ = Et; (IV) R = Me, R¹ = i-Pr;
(II) R = Me, R¹ = Me; (V) R = Et, R¹ = Me;
(III) R = Me, R¹ = Et; (VI) R = i-Pr; R¹ = Et

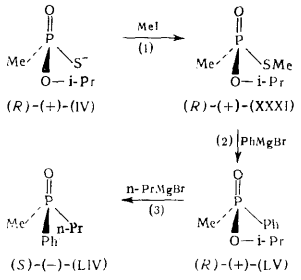
This conclusion was confirmed also by the chemical correlation of the (−)-isomers of *O*-isopropyl methylphosphonothioic (IV) and *O*-ethyl methylphosphonothioic (III) acids:



(26)

(−) (+) (−)
(XXXII) (XXXI)

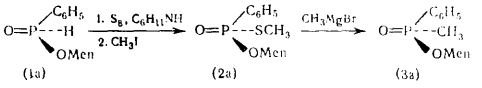
In 1968 Benschop and Boter's group[67] undertook studies whose aim was to determine the absolute configurations of the anticholinesterases obtained from optically active *O*-isopropyl methylphosphonothioic acid (IV); it was therefore necessary to elucidate the absolute configuration of the initial thioacid (IV). Benschop and Boter chose the method of chemical correlation between (+)-*O*-isopropylmethylphosphonothioic acid and (*S*)-(−)-methylphenyl-n-propylphosphine oxide (LIV). Their chemical comparison of the configurations is illustrated below:



(27)

(*R*)-(+)-(IV) (*R*)-(+)-(XXXI) (*S*)-(−)-(LIV) (*R*)-(+)-(LV)

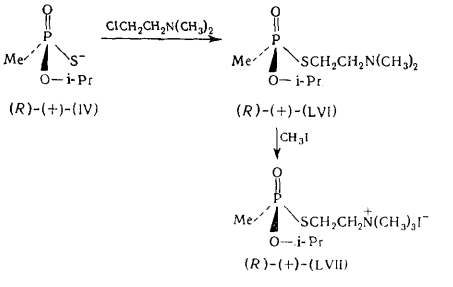
The thioacid (IV) was converted into the phosphine oxide (LIV) by three stereospecific reactions. The first of these (*S*-methylation) proceeds with retention of the configuration at the phosphorus atom[66]. As shown previously[95,96], the third reaction is accompanied by the inversion of the configuration. Consequently the correct determination of the configuration of the (+)-thioacid (IV) requires the knowledge of the stereochemistry of reaction (2):



(1a) (2a) (3a)

Benschop and Boter initially postulated that this reaction proceeds with inversion of the configuration at the phosphorus atom (as in the analogous nucleophilic substitution reactions at the phosphorus atom in similar systems). However, the latest reports[97], which have been confirmed by X-ray diffraction data, indicate that the stereospecific conversion of phosphonothiolates into the corresponding phosphinates proceeds with retention of the configuration at the phosphorus atom§.

Knowing the absolute configuration of the phosphine oxide and the stereochemistry of the successive chemical transformations, the configuration of *O*-isopropyl methylphosphonothioic acid (IV) was determined as (*R*)-(+). The final proof of the correctness of the determination of the absolute configuration of *O*-isopropyl methylphosphonothioic acid was obtained by X-ray diffraction[98] of the *S*-alkyl ester (LVII) synthesised from the (+)-acid (IV) as a result of reactions which do not affect the symmetry of the chiral centre:



(28)

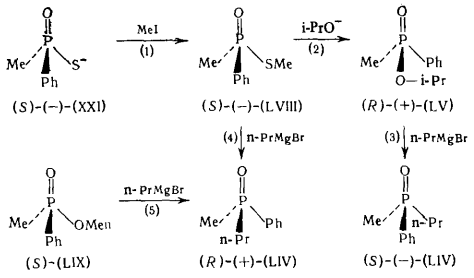
(*R*)-(+)-(IV) (*R*)-(+)-(LVI) (*R*)-(+)-(LVII)

‡ The chemical correlation method involves the determination of the configurations of optically active compounds by chemical reactions which relate compounds of known configuration to those whose configuration is to be determined.

§ The retention of the configuration when phosphonothiolates are acted upon by Grignard reagents has been demonstrated by X-ray diffraction of the phosphonothiolate (2a), which is an intermediate in the conversion of (*R*p)-*O*-menthyl phenylphosphonite (1a) into (*R*p)-*O*-menthyl methylphenylphosphinate (3a).

The absolute configuration of the ester (LVII) was determined by X-ray diffraction as (*R*)-(+), since the initial *O*-isopropylmethylphosphonothioic acid (IV) should also have the (*R*)-(+)-configuration.

Using the same procedure, involving extrapolation to phosphine oxide, Benschop and Boter determined the absolute configuration of methylphenylphosphinothioic acid (XXI):

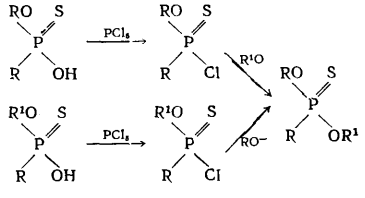


(29)

The acid (XXI) and the phosphinothiolate (LVIII) obtained from it have the same absolute configurations, since *S*-methylation does not affect any of the bonds involving the phosphorus atom. The reaction involving the synthesis of methylphenyl-n-propylphosphine oxide (*R*)-(+)-(LIV) from (*S*p)-menthyl methylphenylphosphinate (LIX) in the presence of n-propylmagnesium bromide [reaction 5, scheme (29)] proceeds with inversion of the configuration. Therefore Benschop and Boter suggested that the similar reaction of isopropyl methylphenylphosphinate (LV) with n-propylmagnesium bromide (reaction 3) also takes place with inversion of the configuration at the phosphorus atom. It is known that the substitution of the methylthio-group by an alkoxy-group (reaction 2) leads to a change in the configuration of the phosphoryl centre. Thus the conversion of (*S*)-(−)-phosphinothiolate (LVIII) into (*S*)-(−)-phosphine oxide (LIV), occurring as a result of two consecutive reactions proceeding with inversion of the configuration, enabled the authors to attribute the absolute (*S*)-configuration to (−)-methylphenylphosphinothioic acid (XXI).

On the other hand, the formation of (*R*)-(+)-phosphine oxide (LIV) on treating (−)-methylphenylphosphinothiolate (LVIII) with n-propylmagnesium bromide proved that, in contrast to *S*-methyl phosphonothiolates, methyl phosphinothiolates react with Grignard reagents, at the same time undergoing an inversion of the configuration at the phosphorus atom.

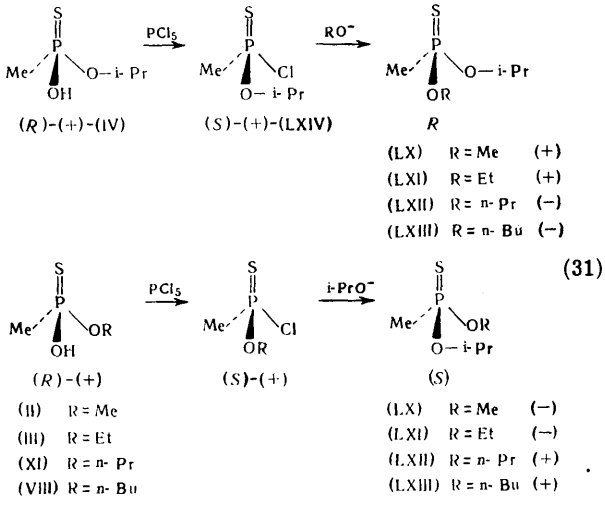
Recently, Mikołajczyk et al.[81] determined the absolute configurations of a series of optically active *O*-alkyl alkylphosphonothioic acids using (*R*)-(+)-*O*-isopropyl methylphosphonothioic acid as the configuration standard. The chemical correlation was based on the stereospecific two-stage conversion of the thioacids into optically active phosphonothionates:



(30)

According to the results of previous studies, both the reaction of the thioacids with phosphorus pentachloride and the substitution of the chlorine atom in phosphonochloridothionates by an alkoxy-group proceed with inversion of the configuration at the phosphorus atom.

The chemical correlation between the configurations of dextrorotatory *O*-alkyl methylphosphonothioic acids is illustrated below:



(31)

(*R*)-(+)-*O*-isopropyl methylphosphonothioic acid (IV) was converted into the (*S*)-(+)-phosphonochloridothionate (LXIV), from which the corresponding optically active *O*-alkyl *O*-isopropyl methylphosphonothioates (LX–LXIII) with the (*R*)-configuration were obtained as a result of reactions with alkoxides RO^- (R = Me, Et, n-Pr, or n-Bu).

On the other hand, the same reactions of (+)-*O*-alkyl methylphosphonothioic acids (II, III, VIII, and XI) (under the influence of PCl_5 and $i\text{-}PrO^-$) yielded the same esters but with rotations of the opposite sign, i.e. with the opposite configurations. Comparison of both types of thionate esters obtained shows that all the *O*-alkyl methylphosphonothioic acids have the (*R*)-(+)-configuration. The chemical correlation between acids of the *O*-alkyl ethylphosphonothioic (I and V) and *O*-alkyl isopropylphosphonothioic (VI and X) series was carried out in the same way.

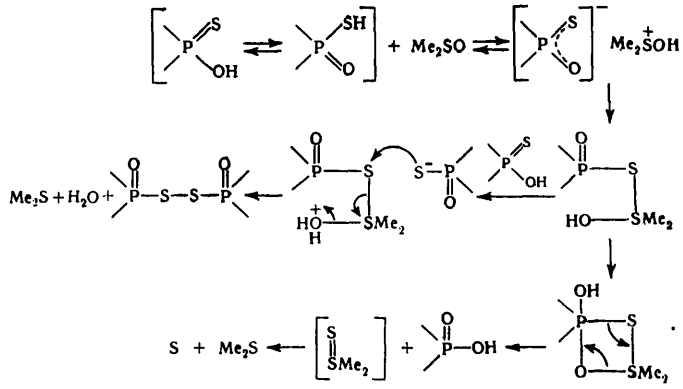
All the results based on chemical correlations show that (+)-*O*-alkyl alkylphosphonothioic acids have the same (*R*)-configuration regardless of the dimensions of the alkyl groups linked directly or by an oxygen bridge to the phosphorus atom.

V. ASYMMETRIC REDUCTION OF SULPHOXIDES BY OPTICALLY ACTIVE PHOSPHORUS-BASED THIOACIDS

Asymmetric syntheses and reactions in which the racemate is resolved kinetically as well as stereospecific transformations are frequently sources of information about the absolute configurations of the optically active reactants. It may therefore be of interest to examine the results obtained by the authors of the review in a study of the asymmetric reduction of chiral sulphoxides with the aid of optically active phosphorus-based thioacids.

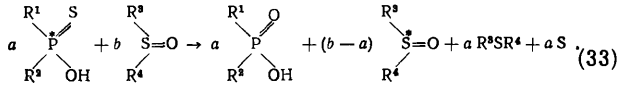
Phosphorus-based thioacids react with sulphoxides in two ways, forming respectively oxygen-containing acids,

sulphides, and elemental sulphur or diphosphoryl disulphides, sulphides, and water[99-102]. The proposed mechanism explained satisfactorily the dual nature of the reaction and the formation of all its products:



(32)

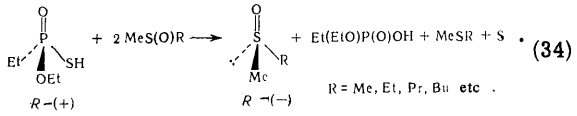
The mode of desulphuration of the acids, usually observed in the presence of an excess of the sulphoxide, constitutes an ideal model reaction for the investigation of the asymmetric reduction of chiral sulphoxides. Mikołajczyk and coworkers[48,102] found that, after the reaction of optically active phosphonothioic acids with an excess of racemic sulphoxides, the sulphoxides which failed to react exhibited optical activity, i.e. had been enriched in the more slowly reacting enantiomers:



(33)

Asymmetric reduction is observed also for equimolar amounts of the reactants and when the reaction has not gone to completion.

It must be emphasised that, regardless of whether the sulphoxide has been used in an excess of in an equimolar amount, the mode of the asymmetric reaction is the same. Thus alkyl methyl sulphoxides with the (S)-configuration always react faster with the dextrorotatory (*R*)-(+)-*O*-ethylphosphonothioate [so that the enantiomer with the (*R*)-configuration predominates after isolation in the sulphoxide which failed to react] and conversely:

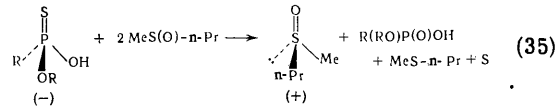


(34)

This has also been confirmed for allyl methyl sulphoxide, whose (–)- and (+)-isomers have, in contrast to simple saturated alkyl methyl sulphoxides, the (*S*)- and (*R*)-configurations respectively.

The above results show that there is a definite relation between the chirality of the optically active thioacid and the chirality of the sulphoxides which react with it. This relation is shown to an even more marked extent in the asymmetric reduction of methyl n-propyl sulphoxide, which has been investigated with the aid of a series of optically active *O*-alkyl alkylphosphonothioic acids. The results of these studies are presented in Table 5.

They show that in all cases the sulphoxide, recovered after the reaction with the (*S*)-(–)-thioacid was dextrorotatory, i.e. contained an excess of the (*S*)-enantiomer, while the sulphoxide regenerated after the reaction with the (*R*)-(+)-thioacid had the *R*-(–)-configuration:



(35)

Table 5. Asymmetric reduction of methyl n-propyl sulphoxide by *O*-alkyl alkylphosphonothioic acids $(RO)R^1P(S)OH$.

No.	R	R^1	Thioacid		Sulphoxide	
			$[\alpha]_D$, °	absolute configuration	$[\alpha]_D$, °	absolute configuration
II	Me	Me	−2.89	*S*	+1.33	*S*
			+2.14	*R*	−1.27	*R*
III	Et	Me	−9.75	*S*	+4.47	*S*
			+10.72	*R*	−3.51	*R*
XI	n-Pr	Me	−1.03	*S*	+0.32	*S*
			+1.30	*R*	−0.35	*R*
IV	i-Pr	Me	−13.9	*S*	+1.29	*S*
			+12.6	*R*	−3.66	*R*
VIII	n-Bu	Me	−12.6	*S*	+3.30	*S*
			+13.02	*R*	−3.34	*R*
V	Me	Et	−8.34	*S*	+2.80	*S*
			+4.70	*R*	−1.78	*R*
I	Et	Et	−13.50	*S*	+5.27	*S*
			+12.90	*R*	−4.92	*R*
X	Me	i-Pr	−13.00	*S*	+0.58	*S*
			−14.67	*R*	−2.17	*R*
VI	Et	i-Pr	+21.54	*S*	+6.45	*S*
			+7.34	*R*	−2.97	*R*

The existence of a definite relation between the chirality of the thioacids and sulphoxides in the reaction being analysed not only demonstrates the possibility of the employment of this reaction to determine the relative or absolute configurations of phosphorus-based thioacids but also consitutes a basis for a model of the transition state in the asymmetric reduction process.

VI. THE APPLICATION OF NMR IN THE DETERMINATION OF THE OPTICAL PURITIES AND CONFIGURATIONS OF OPTICALLY ACTIVE PHOSPHORUS-BASED THIOACIDS

According to general considerations concerning the symmetry of species[103], the groups of nuclei or single nuclei having the same chemical environment either externally or internally, which cannot be interchanged by any symmetry operation, are in a diastereotopic environment in both achiral and chiral solvents. Such nuclei are anisochronic and as a rule should exhibit different chemical shifts and different spin–spin coupling constants. In contrast to these, enantiopic nuclei are screened to the same extent in achiral solvents and are isochronic. However, in chiral solvents or in achiral solvents containing chiral paramagnetic shift reagents, these nuclei become diastereotopic.

These relations make it possible to apply NMR to determine the optical purities of chiral compounds. It permits the determination of the composition of the diastereoisomers obtained from a mixture of enantiomers

and an optically pure reagent (stable diastereoisomers) or to determine the enantiomeric composition in chiral solvents or in achiral solvents containing chiral paramagnetic shift reagents (dynamic diastereoisomeric systems).

The magnetic non-equivalence of diastereoisomers in which the chiral centres are linked covalently in a single molecule was noted for the first time by Mateos and Cram[104]. This phenomenon was used to determine the optical purities of many chiral organic compounds[105,106]. A similar effect was observed by Pirkle and Beare[107] for a mixture of enantiomers in optically active solvents. Here unstable solvation diastereoisomers are formed in consequence of the interaction between the solute and the solvent (for example, as a result of the formation of hydrogen bonds). Because of this, the enantiomers have different chemical environments, which is the reason for the appearance of the magnetic non-equivalence in the NMR spectra.

Pirkle also found that, within the limits of a single class of compounds, the signals corresponding to enantiomers with the same configuration shift in the same direction relative to the signals corresponding to enantiomers with opposite configurations. He called this phenomenon *the sense of magnetic non-equivalence* (*s.m.n.*). Thus, when the signals of the given enantiomer are located in a weaker field, the enantiomer exhibits a "low" *s.m.n.*, while the enantiomer with the opposite configuration is characterised by a "high" *s.m.n.* Knowing the configuration and the *s.m.n.* of a single representative of a given class of compounds, it is possible to determine the configuration of any other compound in this class on the basis of NMR spectra alone.

Diastereoisomeric salts are systems in which there are stronger interactions between the components (acid–base) than in the solvation diastereoisomers investigated by Pirkle. Therefore the NMR spectra of diastereoisomeric salts should presumably also be different and the magnetic non-equivalences $\Delta\delta$ should be more marked.

The magnetic non-equivalence in systems of this type was noted for the first time by Horeau and coworkers[108], who studied the NMR spectra of diastereoisomeric chiral salts of carboxylic acids with optically active α-phenylethylamine.

Mikołajczyk and coworkers[47,109,110], continuing the studies on the absolute configurations of chiral phosphorus-based thioacids, found that they form with optically active amines diastereoisomeric dynamic systems, which give

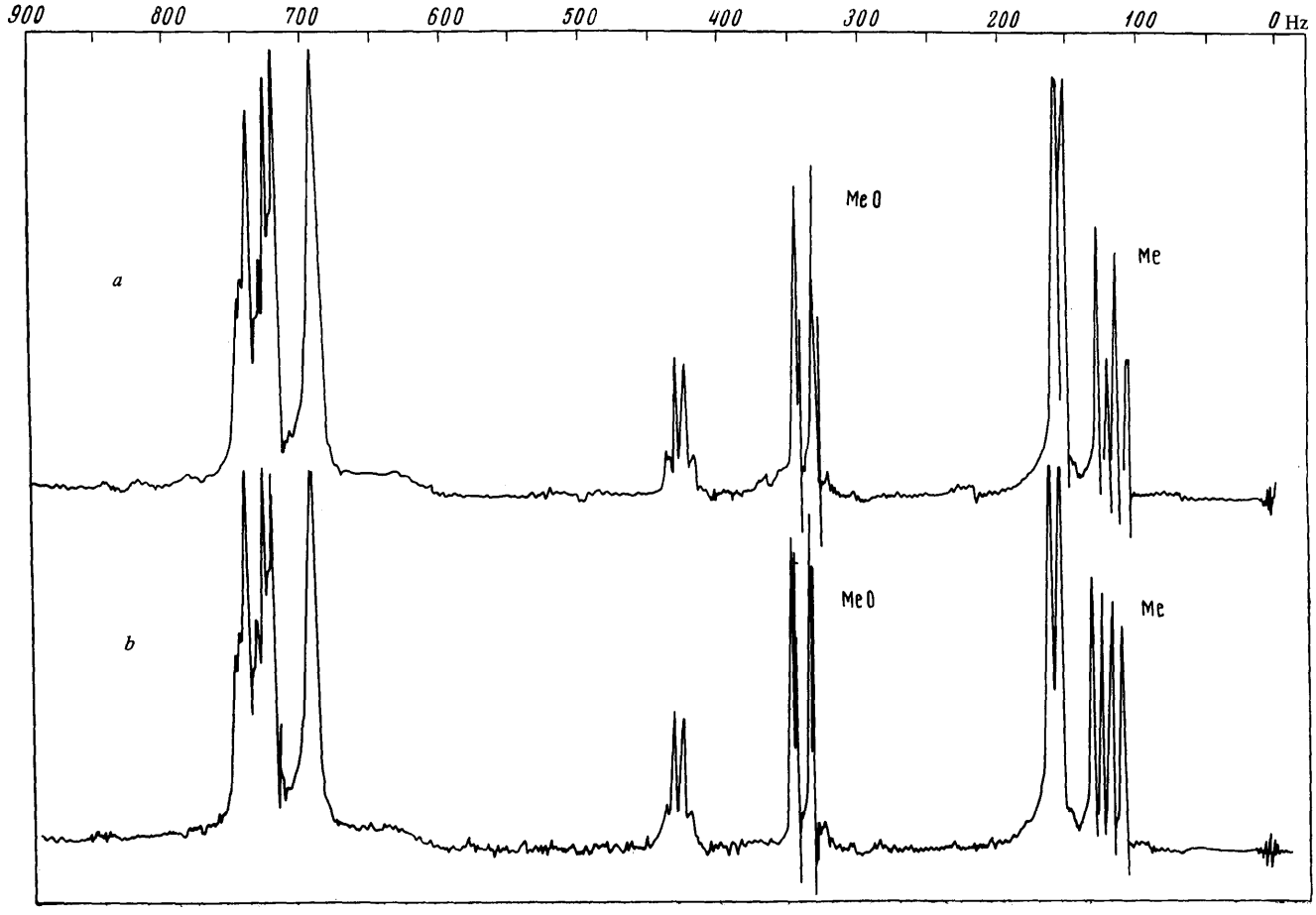
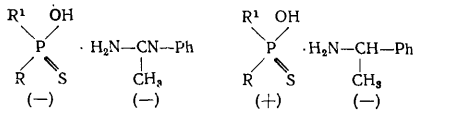


Figure 1. ^{1}H NMR spectra of the diastereoisomeric salts of *O*-methyl methylphosphonothioic acid (II) with (–)-α-phenylethylamine: *a*) 70% of (*S*)-(–)-(II); *b*) racemic (II).

rise to ^{1}H and ^{31}P NMR spectra. Optically active α-phenylethylamine was used in these studies because of the ready availability of both its enantiomers, the ready solubility of its salts in non-polar solvents, and also because they are usually employed for the optical resolution of phosphorus-based thioacids:



The magnetic non-equivalence of *O*-alkyl methylphosphonothioic acids is most effectively observed on the basis of signals due to the *P*-methyl group and that of the class of *O*-methyl alkylphosphonothioic acids on the basis of signals due to the methoxy-group. The ^{1}H NMR spectra of diastereoisomeric salts of *O*-methyl methylphosphonothioic acid presented in Fig. 1 illustrate these two cases.

Fig. 2 presents the ^{31}P NMR spectra of diastereoisomeric salts of *O*-isopropyl methylphosphonothioic acid.

The application of a double resonance technique by Mikołajczyk and Omelańczuk[47,110], as a result of which the ^{31}P NMR spectra of the diastereoisomeric salts are simplified to two single signals corresponding to the enantiomeric acids, merits special attention. Fairly large chemical shifts $\Delta\delta$ are then observed (Table 6), which makes it possible to determine readily the enantiomeric compositions and hence the optical purities of the chiral phosphorus-based thioacids[59,63].

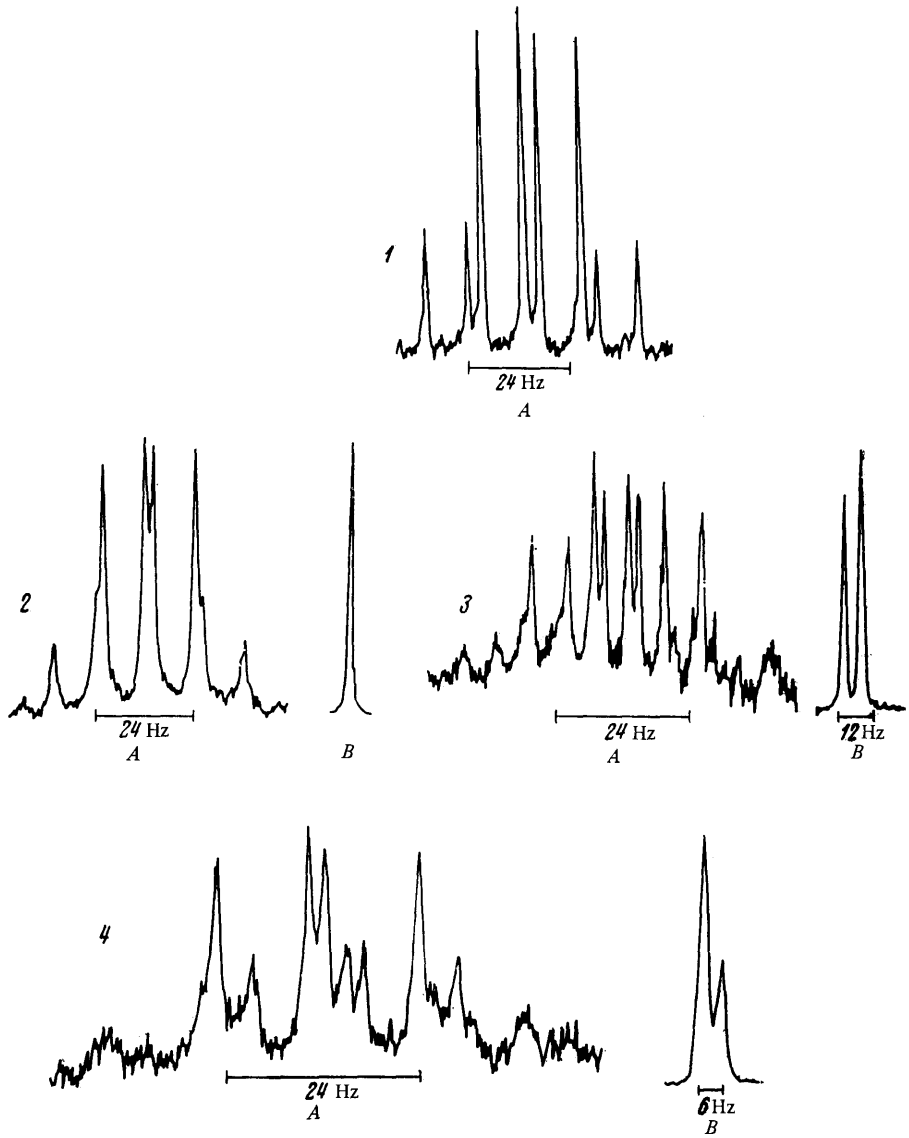


Figure 2. ^{31}P NMR spectra of the diastereoisomeric salts of *O*-isopropyl methylphosphonothioic acid (IV) with α-phenylethylamine (PhEA): *A*) fundamental spectra; *B*) double resonance spectra; 1) (±)-(IV); 2) (±)-(IV).(±)-PhEA; 3) (±)-(IV).(−)-PhEA; 4) (−)-(IV).(−)-PhEA [the thioacid (IV) in which the (−)-enantiomer predominated was used].

Furthermore, it has been noted that a low *s.m.n.* is characteristic of all *O*-alkyl alkylphosphonothioic acids with the (*S*)-configuration and, as for solvation diastereoisomers, remains unchanged within the limits of a single class of compounds. Thus the magnetic non-equivalence of diastereoisomeric salts can also be used to determine the relative or absolute configurations of phosphorus-based thioacids.

Table 6. The magnetic non-equivalences Δδ and *s.m.n.* for the diastereoisomeric salts of phosphorus-based thioacids with (−)-α-phenylethylamine.

Thioacid	Δδ*, Hz ^{1}H NMR**	Δδ, Hz ^{31}P NMR***	*s. m. n.*
Me (MeO) P (S) OH (*II*)	9.2	2.0	low for (*S*)-(−)-
Me (EtO) P (S)OH (III)	18.9	2.1	low for (*S*)-(−)-
Me (i-PrO) P (S) OH (IV)	7.0	6.4	low for (*S*)-(−)-
Me (n-PrO) P (S) OH (XI)	6.9	3.9	low for (*S*)-(−)-
Me (BuO) P (S) OH (VIII)	18.6	3.5	low for (*S*)-(−)-
Et (MeO) P (S) OH (V)	2.9	2.1	low for (*S*)-(−)-
i-Pr (MeO) P (S) OH (X)	0.6	1.2	low for (*S*)-(−)-
t-Bu (MeO) P (S) OH (IX)	4.2	—	—
Et (EtO) P (S) OH (I)	—	2.1	low for (*S*)-(−)-
i-Pr (EtO) P (S) OH (VI)	—	1.1	low for (*S*)-(−)-

* The values of Δδ refer to racemic salts of the thioacids.

** The spectra were obtained on a Varian-HR-60 apparatus in a 60 MHz field in the presence of tetramethylsilane as the internal standard. Groups containing the protons for which the Δδ are quoted have been underlined.

*** The spectra were obtained by a double resonance technique on an INM-60-HL apparatus in a 24.3 MHz field in the presence of phosphoric acid as the internal standard.

The results of studies on the dependence of the magnetic non-equivalence on temperature, the solvent, and concentration[111] suggest that in non-polar solvents there is an acid–base equilibrium:

$$A_RH + A_SH + 2B_R \begin{cases} \xrightarrow{k_1} A_RHB_R \overset{k_3}{\rightleftarrows} A_R^- + B_RH^+ \\ \xrightarrow{k_2} A_SHB_R \overset{k_4}{\rightleftarrows} A_{(S)}^- + B_{(R)}H^+ \end{cases} \quad (36)$$

The undissociated salts, i.e. A_RHB_R and A_SHB_R, the existence of which in the form of ion pairs is favoured by the non-polar medium and the low temperature, are responsible for the observed magnetic non-equivalence. A more detailed mathematical approach to the problem of diastereoisomeric dynamic systems has been described elsewhere[112,113].

The measurement of the magnetic non-equivalence of diastereoisomeric salts has been finding increasing application in the determination of the optical purities and configurations of other chiral compounds[114–118], particularly since the majority of them are in fact resolved by the classical method involving the crystallisation of diastereoisomeric salts.

VII. CIRCULAR DICHROIC STUDIES ON OPTICALLY ACTIVE PHOSPHORUS-BASED THIOACIDS

Following the development of accurate spectrophotometric apparatus, methods for the determination of configurations based on the use of the phenomenon of optical rotatory dispersion (ORD) and circular dichroism (CD) have assumed increasing importance recently[119]. Since CD spectra are more readily susceptible to analysis, particularly for complex organic molecules containing various functional groups, CD is more widely used to determine the configurations of chiral molecules. CD spectra for optically active phosphorus-based thioacids yielded valuable information and confirmed the validity of the configurations[120] assigned by other methods.

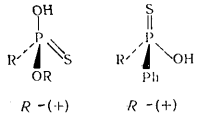
Table 7. The specific rotations $[\alpha]_D$, circular dichroic data, and ultraviolet spectroscopic parameters for *O*-alkyl alkylphosphonothioic acids R(R^{1}O)P(S)OH.

Thioacid R	Thioacid R^1	$[\alpha]_D$ °	Absolute configuration	Solvent	CD: λ_{max}, (nm (Δε)	u.v.: λ_{max}, nm (ε)
Me	Me	+2.8	*R*	isooctane	197 (−1.3)	—
				water	202 (−2.3)	—
Me	Et	+9.5	*R*	isooctane	196 (−2.9)	—
				water	205 (−2.3)	—
Me	n-Pr	+1.3	*R*	isooctane	195 (−0.86)	—
				water	201 (−0.66)	—
Me	i-Pr	+14.7	*R*	isooctane	196 (−3.3)	—
				acetonitrile	197 (−1.5)	—
				ethanol	197 (−1.8)	—
Me	n-Bu	−12.6	*S*	isooctane	198 (+4.4)	—
				water	204 (+2.8)	—
Et	Me	−8.3	*S*	isooctane	199 (+5.2)	190 (9900)
				water	205 (+3.4)	206 (5600)
				ethanol	200 (+1.8)	190 (10 500)
Et	Et	+12.9	*R*	0.5 *N* HCl	200 (+2.7)	—
				isooctane	197 (−2.3)	—
Et	Et	−13.9	*S*	isooctane	197 (+2.3)	—
				ethanol	198 (+1.4)	—
				water	205 (+1.5)	—
i-Pr	Me	−17.0	*S*	water-KOH (pH 12)	213 (+1.3)	—
				isooctane	198 (+2.9)	—
				water	204 (+1.8)	—
i-Pr	Et	−21.3	*S*	isooctane	198 (+4.2)	—
				water	205 (+2.6)	—
t-Bu	Me	+13.2	*R*	isooctane	200 (−5.7)	190 (7150)
				ethanol	202 (−3.5)	185 (8200)
				water	210 (−4.4)	196 (5800)
						207 (4950)
						185 (7700)

The CD spectra for all the *O*-alkyl alkylphosphonothioic acids investigated exhibit only one intense transition near 200 nm, which is shown most distinctly in non-polar solvents. The values of Δε and χ_{max} are listed in Table 7. Evidently the negative Cotton effect is characteristic of acids with the (*R*)-(+)-configuration and the positive effect is characteristic of acids with the (*S*)-(−)-configuration. The position of the absorption band is almost independent of the type of solvent and a distinct bathochromic shift is observed only in water. This is probably a result of the dissociation of the acids P(S)OH and a change in the nature of the chromophoric group.

The CD spectra for alkylphenylphosphinothioic acids (XXI and XX) are much more complex owing to the presence of an aromatic ring in the molecule and contain at least four absorption bands in the region near 270,

230, 215–220, and below 200 nm. The second band can be attributed to the chromophore P(S)OH. It has been observed that both phosphinic acids investigated, with the same signs of optical rotation, are homochiral, i.e. have the same configuration:



R -(+) *R* -(+)

It is noteworthy that the application of conformational asymmetry rules[121] leads to the same conclusion, namely that (+)-*O*-alkyl alkylphosphonothioic and (+)-alkylphenylphosphinothioic acids have the (*R*)-configuration and exist in solution in the thiono-form.

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Chemical Effects of Heat on Cellulose

O.P.Golova

The mechanism of rupture of the glucosidic bond in the thermal decomposition of cellulose is examined, and data are given on the primary steps of formation of levoglycosan. The effect of inorganic components on carbon-carbon bond rupture and on the direction of decomposition is considered. Possible practical uses of the results are discussed.

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I. INTRODUCTION

The thermal decomposition of cellulose in a vacuum, with the formation of 1,6-anhydro-β-glucopyranose, was first accomplished in 1918 by Picter and Sarasin[1]. Interest in this process has continued to the present time; this can be ascribed to its importance from both scientific and practical points of view.

The thermal decomposition of cellulose to the monomeric levoglycosan involves formation of a new 1,6-anhydro-bond replacing the ruptured 1,4-carbon–oxygen–carbon bond (with preservation of the composition of the monomer unit of cellulose); during this process at 300° to 400°C cellulose retains its hydroxy-groups. Furthermore, thermal breakdown involves formation of a new conformation of the glucopyranose unit, with transition from $C-1$ to $1-C$ and of all the hydroxyls from equatorial to axial positions. Investigations of the thermal decomposition of cellulose are of interest for establishing its mechanism, in assessing the possibility of controlling thermal changes in cellulose (which may occur both in its extraction and in the exploitation of cellulosic materials), and also for producing new and more thermostable materials.

Surveys have been published[2,3] of research undertaken between 1918 and 1970 on the thermal decomposition of cellulose in a vacuum. However, Shafizadeh's review[2] has several important defects. In particular, it ignores results obtained on the mechanism[4-8], including data on the rates of the process and its possible retardation[5,8]. Furthermore, on the fundamental question of obtaining a high yield (up to 73%) of levoglycosan by the thermal decomposition of cellulose Shafizadeh refers to the work of Sandermann and Augustin published[9] in 1964, whereas analogous results had appeared[5] as early as 1960. Černý and Staněk's review[3] paid very little attention to the problem of obtaining levoglycosan by the thermal degradation of cellulose. The mechanism is not analysed, the reviewers merely mentioning that it should be analogous to that of the acid cleavage of glycosides. Rogovin's monograph[10] also makes a one-sided approach to the mechanism of the thermal breakdown of cellulose to levoglycosan. The author considers merely a radical mechanism on the basis of Arthur's results[11].

Thus until recently the mechanism of the thermal decomposition of cellulose to levoglycosan had not been sufficiently fully and objectively discussed. The aim of the present Review is to give the modern view of the mechanism of thermal breakdown with the formation of 1,6-anhydro-β-D-glucopyranose (levoglycosan) and other anhydro-sugars. Special attention will be paid to a critical assessment of work during the last five or six years, taking into account earlier investigations on these lines. Research on the further degradation of the monomer units of cellulose is not considered in this Review.

II. MECHANISM OF RUPTURE OF A GLUCOSIDIC BOND IN THE THERMAL DECOMPOSITION OF CELLULOSE

(*a*) Transglucosidation

Recent publications[12,13] reveal no generally accepted view on the mechanism of rupture of a glucosidic bond with subsequent formation of 1,6-anhydro-β-glucopyranose (levoglycosan) and other products of the action of heat on cellulose. Two mechanisms of cleavage of the cellulose molecule—homolytic with the formation of free radicals or heterolytic to give intermediate carbonium ions with subsequent formation of 1,2-, 1,4-, and 1,6-anhydrosugars—have been suggested. Shafizadeh and his coworkers[12,14,15] regard these mechanisms as somewhat hypothetical, and insufficient experimental evidence is available to support either. Furthermore, a single route for formation of each decomposition product is thought to be improbable under pyrolytic conditions. Under normal conditions chemical reactions follow the path of minimum energy consumption, and the solvent plays a considerable part in the transfer of ionic charges, while contributing to intramolecular interactions. During pyrolysis, however, many molecular rearrangements and reactions may be taking place simultaneously. It follows from general considerations that the pyrolytic degradation of the cellulose molecule should involve fission of a glucosidic bond or dehydration and breakdown of anhydroglucose units. Shafizadeh et al. used a combination of physical and chemical methods, including thermogravimetric analysis, to obtain a deeper insight into the complicated thermal reactions of hydrocarbons. Spectroscopic methods were also used, as well as modern methods of chemical and radiochemical analysis of the decomposition products. Radiochemical analysis was applied to the products obtained from levoglycosan labelled with carbon-14 and from its

polymer. The above combined approach was used initially to study the thermal decomposition of model compounds [16-18]. Several phenyl and substituted phenyl 2-amino-2-deoxy-β-D-glucopyranosides and various acetylated phenyl glucosides were examined with the aim of determining the effect of substituents in the sugar molecule and the accessibility of free hydroxy- and amino-groups [17].

Table 1. Analysis of volatile products of the pyrolysis of various phenyl glycosides [17].

Phenyl glycoside	Free phenols, %	Initial compound, %
β-D-Glucopyranoside	100	0
2-Amino-2-deoxy-β-D-glucopyranoside	82	2
2-Acetamido-2-deoxy-β-D-glucopyranoside	99	0
2-Deoxy-β-D-*arabino*-hexopyranoside	82	4
2-Acetamidotri-*O*-acetyl-2-deoxy-β-D-glucopyranoside	29	42
Tetra-*O*-acetyl-β-D-glucopyranoside	0	62
Tri-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranoside	0	63

We must consider in greater detail the experimental results on the thermal decomposition of phenyl glucosides, since they form the basis of the suggested mechanism of rupture of the glucosidic bond with subsequent formation of anhydro-sugars. Table 1 gives analyses of volatile products from the pyrolysis of various glucosides. The model compounds used show that the pyrolytic reactions involve rupture of glucosidic bonds. The aglycone group abstracts a proton with the liberation of phenol, which is removed, while the glycosyl group forms the anhydro-sugar or condenses to randomly combined oligosaccharides. Thermal analysis, together with analytical data on the pyrolysis products, indicates that acetylated phenyl glucosides are considerably more stable than the original compounds. Table 1 shows also that free hydroxyls play an important role in the thermolysis of glucosides: almost 100% of phenol is formed by rupture of the glucosidic bond in phenyl β-D-glucopyranoside; yet this bond is stable when the hydroxy-groups have been substituted (phenyl tetra-*O*-acetyl-β-D-glucopyranoside), and phenol is not formed, up to 62% of the starting material remaining unchanged.

From the thermal analysis together with an analysis of the distillation products it was concluded that thermolysis involved intramolecular transglucosidation. Since thermal reactions are less specific, various hydroxyls may take part. Substitution of hydroxyls in the aglucone or the glucosyl moiety may affect the accessibility, i.e. the reactivity, of the sites of glucosidation. Products of the pyrolysis of polymers obtained from levoglycosans labelled with carbon-14 at $C_{(1)}$, $C_{(2)}$, and $C_{(6)}$ were separated by thin-layer chromatography and then subjected to radiolysis [18]. The results suggested that thermal decomposition involved rupture of a glucosidic bond, opening of the cyclic structure, and subsequent fragmentation of the monomer unit of cellulose. The formation of two molecules of formaldehyde from the anhydroglucose unit was shown to result from the $C_{(1)}-C_{(5)}$ fragment of levoglycosan. It was found also that the production of a 3,6-anhydro-ring leads to the formation of furyl methyl ketone, whose decomposition yields furaldehyde from the $C_{(2)}-C_{(6)}$ fragment of the monomer unit. These investigations showed the identity of products obtained in the pyrolysis of cellulose and polymeric levoglycosan with analogous isotopic labelling.

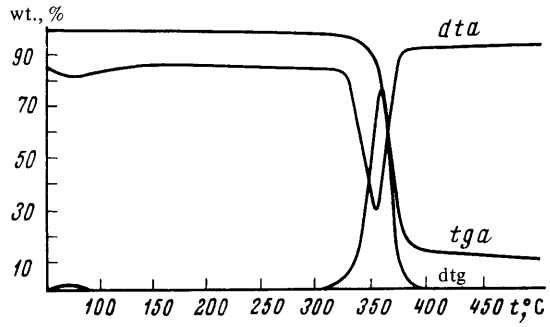

Figure 1. Thermogram of untreated cellulose.

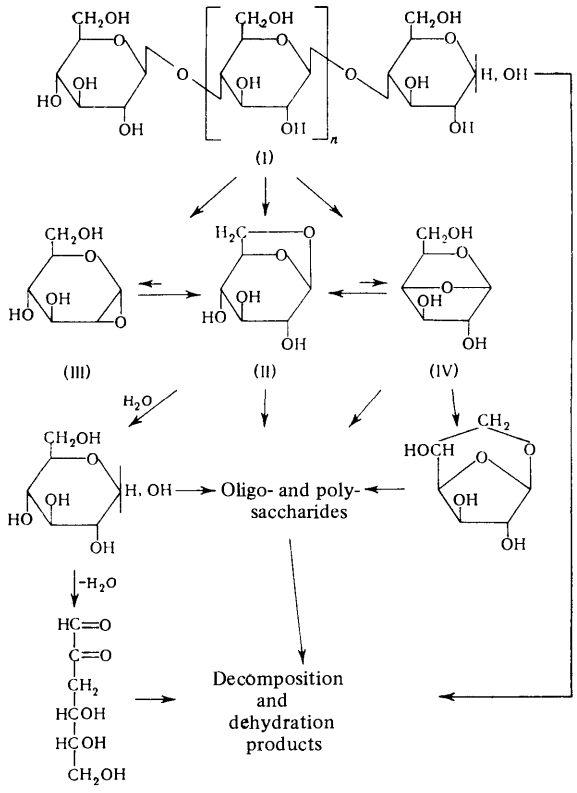

Figure 2. Pyrolysis of cellulose and transformation of products.

Developing their investigations on the thermal decomposition of carbohydrates [14-18], these workers used in a later study [12] a combined approach (previously applied to model compounds) to examine the mechanism of the thermal decomposition of cellulose. Fig. 1 illustrates the principal results, and Table 2 gives the composition of the pyrolysis products. The curves show that these reactions occur very slowly up to 300°C, after which they accelerate (when the temperature becomes high enough for rapid rupture of the glucosidic bond and distillation of the products). Thermogravimetric analysis (Fig. 1) and identification of the pyrolysis products from data obtained with model compounds [14-18] lead to the conclusion [12] that such rupture occurs by a transglucosidation mechanism involving one of the three free hydroxyls. Theoretically the 2-, 3-, or 6-hydroxyl might be involved in intramolecular transglucosidation, with fission of the $C_{(1)}-C_{(4)}$ polymer bond. This produces a new terminal group with an unsubstituted 4-hydroxyl, which in turn may be involved in further transglucosidation during pyrolysis. The suggested mechanism is set out in Fig. 2.

Table 2. Composition of pyrolysis products (% on initial quantity of cellulose) obtained in a stream of nitrogen at 300°C.

Product	Pressure	
	1 atm	5 mmHg
Product of distillation (tar)	19.1	55.8
Levoglycosan	3.57	28.1
1,6-Anhydro-β-D-glucofuranose	0.38	5.6
D-Glucose	traces	traces
Hydrolysable material	6.08	20.8

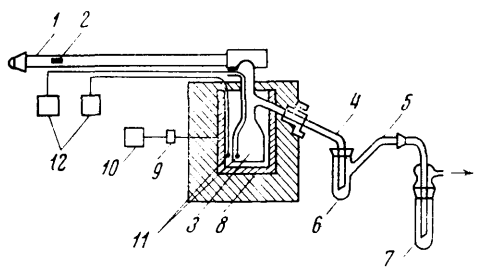

Figure 3. Diagram of apparatus for the thermal treatment of cellulose: 1) tube for keeping cellulose in a vacuum at room temperature; 2) core of magnet (for transferring cellulose to reaction vessel); 3) reaction vessel; 4) connecting tube with condenser; 5) connecting tube; 6) receiver for pasty distillate; 7) receiver for liquid and volatile products; 8) furnace block; 9) thermocouple for temperature control; 10) millivoltmeter; 11) measuring thermocouples; 12) d.c. potentiometer.

(*b*) Homolytic Rupture

A combination of different methods must be used to study the mechanism of thermal decomposition of a polymer, as is known from the chemistry of macromolecular compounds [19-21]: the mechanism can be assessed only from the totality of the results. Investigations on the thermal breakdown of cellulose took place in three stages.

The process was studied initially in a high vacuum (10^{-5} mmHg) by examining the effects of several factors—temperature, residual pressure, design of apparatus, degree of polymerisation of the original cellulose, and additions of glucose—on the yield of levoglycosan in the apparatus illustrated in Fig. 3 under conditions which ensured that this was the main product [4]. During an experiment the vacuum was maintained at 10^{-5} mmHg and the temperature at 305 ± 1°C (after the initial 5–10 min). The products were analysed after 10, 20, 40, 90, and 300 min, when the proportions of cellulose that had decomposed were 2–4%, 10%, 30%, 50%, and 80% respectively. The design of apparatus and the experimental conditions were published somewhat later [4]. The experiments established that conditions for obtaining a constant and quite high yield of levoglycosan (50–60% on the weight of cotton cellulose) [22,23]. The yield was independent of the degree of polymerisation of the initial cotton cellulose over the range 1000–150, [24] and was lowered considerably by the addition of glucose to the cellulose [25].

Subsequent investigations were aimed at establishing the mechanism of the thermal breakdown of cellulose to levoglycosan. It had originally been shown [27] that the yield of this compound from β-D-glucose and from cellobiose is far lower than from cellulose with degrees of polymerisation 1000–150 (respectively 14%, 5%, and 50%). [24] The addition of glucose to cellulose lowered the yield of levoglycosan [25]. Thus the hypothesis that levoglycosan is formed under pyrolytic conditions by the hydrolysis of cellulose to glucose followed by dehydration of the latter was not confirmed [27].

More recent examination [28] of the composition of the distillate from the thermal decomposition of cellulose has established that the formation of 3–4% of 1,6-anhydro-β-glucofuranose accompanies the levoglycosan. The former compound was present (8%) also among the thermal decomposition products from glucose, and was accompanied by 2–3% of phenols. Special experiments undertaken to establish the presence of 1,4-anhydroglucopyranose and of its 2,3,6-trimethyl derivative among the thermolysis products from cellulose and from trimethylcellulose respectively were unsuccessful. According to a personal communication, Shaw regards the formation of 1,4-anhydroglucopyranose and its trimethyl derivatives as impossible for steric reasons.

It was thus established that under certain conditions levoglycosan is the main product of the thermal decomposition of cellulose. However, neither the results nor the identification of volatile products were sufficient to assess the mechanism of breakdown of the polymeric molecule. Subsequent studies were therefore concerned with the changes in the cellulose molecule itself produced by heat and with the distillation products. Attention was concentrated on the following characteristics—(i) the quantity of chemically unchanged monomer units in the cellulose, (ii) the degree of polymerisation, (iii) the content of formyl and carboxyl functional groups, (iv) the physical structure of heat-treated specimens, (v) the yield of levoglycosan, and (vi) the rate of the process (and its possible inhibition).

A marked difference in yields of levoglycosan—50% and 3–4% respectively—was found when cotton cellulose and cellulose hydrate were heated [4]. This was originally attributed to a difference in the physical structure of the celluloses, but it was subsequently demonstrated [5] that the quantity and the composition of ash elements present in

the cellulose affect the path of decomposition and hence the yield of products. After the ash content of both specimens had been reduced to < 0.002%, the yield of monomer on thermal decomposition amounted to 73% of the cellulose decomposed for both modifications[5]. The results indicated that a hydroxylated polymer (cellulose) is capable of thermal depolymerisation at the glucosidic bonds[5] and permitted an approach to a study of the mechanism (apart from the effect of salt cations, whose role has been discussed separately[5,30,31]).

Table 3. Thermal decomposition of cotton cellulose (ash content 0.05%)*.

N, %	*W*, %	*n*	*M*, %	Content	
				C, %	H, %
0	—	2000—700	99.4	44.4	6.17
2	5	400	99.4	44.4	6.17
3	10	200	87.0	44.4	6.17
10	40	200	80.4	44.9	6.17
36	50	200	80.4	45.0	6.2
64	45	200	52.7	51.5	5.5
86	40	200	7.7	67.5	4.7

*N = degree of decomposition (% on initial cellulose);
W = yield of levoglycosan (% on cellulose decomposed);
n = degree of polymerisation;
M = content of chemically unchanged monomer units.

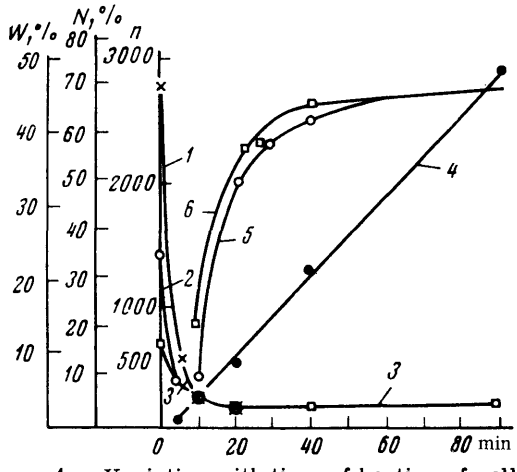

Figure 4. Variation with time of heating of cellulose [see footnote to Table 3)]: 1) n (initially 2800); 2) n (1500); 3) n (700); 4) N; 5) W (n = 2800); 6) W (700 obtained by partial hydrolysis).

Table 3 presents data on the quantity of cellulosic units remaining unchanged in specimens that have been heated for various times. A striking fact is that levoglycosan is formed in low yield (5—10% of the cellulose decomposed) from a cellulose containing 99.4% of monomer units chemically unchanged in the initial stages of decomposition. Quite a high proportion of monomer units remain chemically unchanged almost throughout the decomposition of cellulose: only at ~90% decomposition does the quantity of unchanged units fall to ~8%.[4,5]

Results for the time variation of the degree of polymerisation of cellulose[4,6] are given in Table 3 and illustrated by Figs. 4 and 5. The latter show that decomposition begins with a sharp decrease in n with losses in weight of 5% and 20—30% for cotton cellulose and cellulose hydrate respectively. After this, the degree of polymerisation remains constant up to 80% decomposition, at 200—300 and 30—50 for the two modifications[5]. These limiting values of n agree with those obtained in the heterogeneous hydrolysis of cellulose. The first stage of the process is characterised by a low yield of levoglycosan and a sharp drop in the degree of polymerisation; the second stage gives a high yield, which n remains constant.

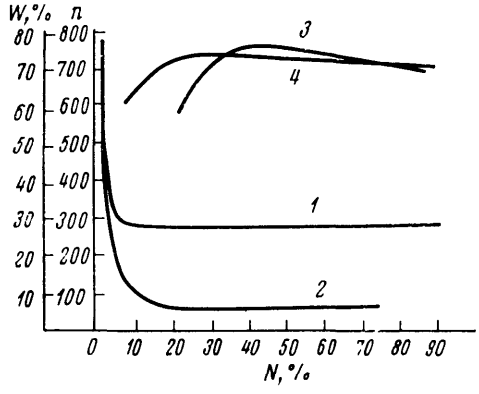

Figure 5. Influence of degree of decomposition N on: 1) n for cotton cellulose; 2) n for cellulose hydrate; 3) W for cotton cellulose; 4) W for cellulose hydrate (ash content < 0.002%).

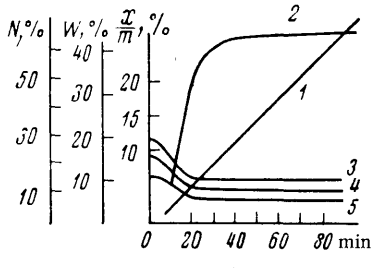

Figure 6. Time variation of: 1) N; 2) W; and sorption capacity x/m (where x is the quantity of moisture and m the weight of the specimen) at different relative humidities (p_1/p_0, %): 3) 90; 4) 80; 5) 60.

The results can be interpreted on the basis that the cellulose molecule is a periodic aggregation of segments of differing structure. The first stage of thermal decomposition involves rupture of the chain links with the accumulation of fragments having degrees of polymerisation of 200—300 and 30—50 for cotton cellulose and cellulose hydrate respectively. Dehydration predominates at this stage, followed by far-reaching breakdown of the

monomer unit with the formation of volatile products (yield of levoglycosan only 5–10%) (Figs. 4 and 5). The yield of levoglycosan reaches its maximum value in the second stage, after the degree of polymerisation has become constant, when thermal decomposition involves the consecutive chemical conversion of monomer units of the cellulose fragment accompanied by detachment of a monomer unit, which is converted by internal isomerisation into levoglycosan. The degree of polymerisation is maintained at 200 with degrees of decomposition of the cellulose from 4% to 70–80% (Table 3), and remains unchanged in a vacuum at 300°C for 80 min.

In this connection it is interesting to consider the light thrown on the physical structure of cotton cellulose by the water-vapour sorption isotherms obtained during heat-treatment [32]. Fig. 6 shows that the sharp drop in the degree of polymerisation to limiting values (which represents a sharp increase in the yield of levoglycosan) is accompanied by a fall in the sorption capacity of cellulose during the first few minutes of heat-treatment. Both the sorption capacity and the yield of levoglycosan then remain constant. These facts indicate that in the first stage the cellulose chain breaks down mainly in amorphous regions.

Table 4. Variation in content of carboxyl and carbonyl groups during the thermal decomposition of cotton cellulose [4].

N, %	Content, %		n	N, %	Content, %		n
	COOH	CO			COOH	CO	
0	0.02	0.26	800	3	0.05	0.80	200
1	0.02	0.35	400	7	0.10	0.78	200
2	0.03	0.75	200	30	0.32	0.87	200

In order to characterise the two-stage breakdown of cellulose to limiting degrees of polymerisation it was important to trace the variation in the content of functional groups with the time of heat-treatment under conditions of maximum inhibition of oxidising processes (10^{-5} mmHg vacuum). [4] Table 4 shows that the rapid change in degree of polymerisation in the first stage of decomposition is not accompanied by a change in the content of functional groups. In the second stage the numbers of carboxyl and carbonyl groups increase, while the degree of polymerisation remains constant. Thus these groups do not become weak points in the cellulose molecule right until limiting degrees of polymerisation.

The rate of the process was then studied [5] by means of a McBain spring balance specially equipped for decomposition studies at 300–400°C. Figs. 7 and 8 show the rate curves for cotton cellulose and for cellulose hydrate with an ash content < 0.002%, when the curves are similar in shape with maxima within the same limits of decomposition. Decomposition occurs quite fast, with maximum rates per minute of 2% and 3% respectively for the cotton cellulose and cellulose hydrate decomposed. Fig. 9 illustrates the possibility of slowing down the thermal decomposition of cellulose, such retardation being accompanied by an intensification of secondary processes of extensive decomposition [8].

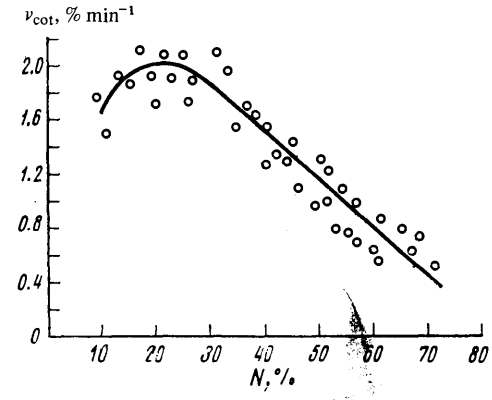

Figure 7. Rate v_{cot} of thermal decomposition of cotton cellulose (ash content < 0.002%).

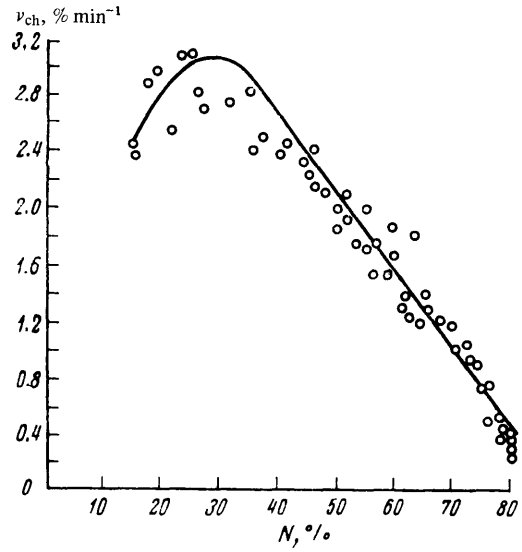

Figure 8. Rate v_{ch} of thermal decomposition of cellulose hydrate (ash content < 0.002%).

It is noteworthy that, while cellulose hydrate has degrees of polymerisation of 30–50, compared with the 200–300 of cotton cellulose, its rate of decomposition exceeds that of the latter by 50%. This indicates the importance of the absolute number of terminal monomer units in thermal decomposition. All segments of the polymer molecule are equally accessible to the action of heat in both modifications, so that the differences observed in the quantities of cellulose decomposed at the first stage, in the limiting degrees of polymerisation, and hence in the rates of the process are determined by the structural inhomogeneity of the cellulose macromolecules themselves and by their different proportions of amorphous and crystalline regions. Formation of levoglycosan—the principal route of thermal decomposition—takes place in the second stage (with the degree of polymerisation constant) after removal of the amorphous regions of the cellulose.

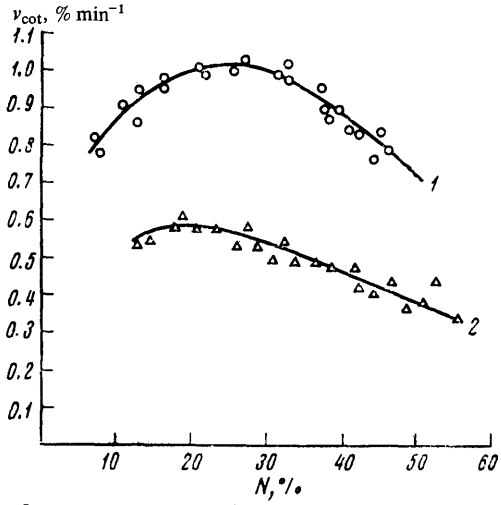

Figure 9. Rates v_{cot} of thermal decomposition of cotton cellulose: 1) in absence of an inhibitor; 2) in presence of an inhibitor.

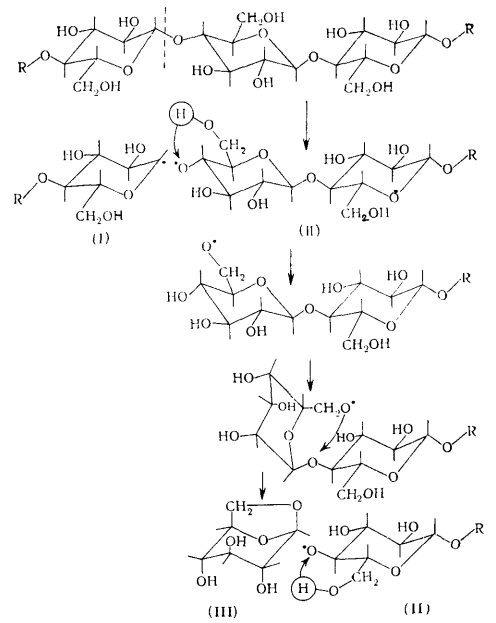

Figure 10. Scheme of depolymerisation of cellulose by a radical–chain mechanism, in which (I) and (II) are radicals.

The high rates with a high yield of levoglycosan, the constancy of the degree of polymerisation of cellulose throughout the decomposition following an initial sharp fall to a limiting value, and also the possibility of slowing down the process by means of radical inhibitors suggest that the thermal depolymerisation of cellulose can be regarded as a radical–chain process which, having begun in some activated region of the macromolecule, leads to the complete breakdown of cellulose with the detachment of one glucose anhydride molecule after the other from the initiated end of the chain. It was suggested[5,7] that the appearance of an active centre in a monomer unit tends to weaken the glucosidic bond nearest to the glucose unit, and its rupture leads to the appearance of a new active centre (Fig. 10). Change in conformation of the monomer unit makes isomerisation possible, leading to the formation of glucose anhydride (levoglycosan) molecules.

Table 5. Effect of an inhibitor (di-2′-naphthylphenylenediamine) on yield of levoglycosan from the pyrolysis of cellulose[35].

Inhibitor, mole %	Yield, %
0.00	34±3.0
0.90	26.0±2.0
2.25	17.4±3.0
4.50	4.4±2.0

Kislitsyn and his coworkers[33–36] paid special attention to the choice of a suitable inhibitor for the thermal decomposition of cellulose, and selected di-2′-naphthylphenylene-diamine, a well known inhibitor of free-radical reactions. With an inhibitor concentration of 4.5 mole % the yield of levoglycosan is 4.9% on the cellulose, instead of the 36.4% obtained in a control experiment (Table 5). The justification of the transition of a monomer unit from the $C-1$ to the $1-C$ conformation[34] is especially interesting. Kislitsyn remarks that the very fact of the formation of levoglycosan in the $1-C$ conformation is convincing evidence of the changes occurring during thermolysis. The energy barriers opposing the transitions are low, and are easily overcome even by thermal motion. The difference in energy observed between the chair and boat conformations of cyclohexane is only 5.3 ± 0.3 kcal.[35,36] The main problem is whether the terminal monomer unit is situated in the limited space of the crystallite between the cellulose chains after transition to the $1-C$ conformation. In a crystalline zone the planes containing the chains are 3.95 Å apart[34]. Calculations and measurements on a model show that after such a transition the terminal unit is located about 2.5 Å above the plane of the chain. A vacant space >1 Å high separates the adjacent planes. Conformational changes can therefore occur without steric hindrance.

(*c*) Mechanism of Rupture of a Glucosidic Bond in the Thermal Decomposition of Cellulose

Recent results have led to a denial[12] of a homolytic mechanism for rupture of the glucosidic bond, which was attributed to intramolecular rearrangements, i.e. transglucosidation of a free hydroxy-group with subsequent formation of levoglycosan. This mechanism was based mainly on experiments with model compounds[15–18] and also on thermographic results and identification of the thermal decomposition products from cellulose. It is extremely significant that the role of free hydroxyls in the thermal rupture of a glucosidic bond was shown convincingly on model compounds having different degrees of substitution

of their hydroxy-groups. The results provide a good illustration that protecting the hydroxy-groups almost changes the direction of the process.

These results will also explain the different directions of thermal decomposition in amorphous and in crystalline regions of cellulose [6,32], where the change in direction depends on the blocking of hydroxy-groups by hydrogen bonds. Thus intramolecular rearrangement may predominate in monosaccharides and probably disaccharides, in which hydrogen bonds are absent, and the glucosidic bond may be ruptured by the mechanism shown in Fig. 2.

These conclusions are consistent with the hypothesis [6] that the thermal decomposition of cellulose takes place in two stages. In the first stage (in the amorphous regions) dehydration occurs, and a small quantity of levoglycosan (5–10% based on the cellulose decomposed) may be formed by transglucosidation at the carbon-(6) atom [5,6,32]. This stage involves a decrease in the molecular weight to that corresponding to the limiting degree of polymerisation. The postulate that all hydroxyls are equivalent in decomposition by a transglucosidation mechanism would have suggested a continuous decrease in the molecular weight of cellulose, which is not observed in practice. A second characteristic feature [5] is the increasing rate of the process, which passes through a maximum. With equal accessibility of the hydroxy-groups (Fig. 2) there is no reason to expect intramolecular rearrangements to show a maximum rate. Extremely significant evidence of a homolytic process is provided by the possibility of slowing down decomposition [8,34,35], which could not be achieved with a heterolytic process.

The mechanism shown in Fig. 2 is based on extremely interesting results [17] on the thermal decomposition of phenyl glucosides and their derivatives. The monomer units of cellulose were considered [12] in isolation from the actual polymer and existing intermolecular interactions, and the mechanism of the formation of levoglycosan was regarded as analogous to reactions occurring in monosaccharides. However, there is little justification for transferring the mechanism of rupture of a glucosidic bond in a monomeric compound to the cellulose polymer, with its supermolecular structure, inhomogeneity of physical structure, and hydrogen bonds blocking hydroxyls in crystalline regions. The absence of radicals in the thermal decomposition of corresponding model compounds of anhydro-sugars [12] is no proof of their absence in the rupture of a glucosidic bond in cellulose. Decomposition of the latter, because of its polymeric nature, may take place by a mechanism differing from that of the degradation of a disaccharide. As noted above, the yields of levoglycosan from cellulose and from cellobiose under the same conditions were respectively 50% and 4%. [26] Such a difference in behaviour between a dimer and a polymer was explained by the influence of the supermolecular structure of the latter (hydrogen bonds and other intermolecular interactions). The effect of hydrogen bonds on the reactivity of hydroxyls in oxidation, etherification, etc. is well known.

Identification of the products of thermal decomposition has also suggested a mechanism. Using modern methods (chromatography, mass spectrometry, etc.) Shafizadeh et al. detected in the distillate 1,6-anhydro-β-D-glucopyranose and also 1,6-anhydro-β-D-glucofuranose, which had been found previously [28,37]. The presence of 3-deoxy-D-*erythro*-hexulose in the distillate has been established for the first time; it is assumed to be formed from glucose (Fig. 2). Thirty-seven different volatile products—among them acids (lactic, acetic, formic), aldehydes, ketones, water, carbon monoxide, and carbon dioxide—had been detected somewhat earlier [38], also by gas–liquid chromatography, among the products of the pyrolysis of cellulose at 375°C.

However, conclusions on the mechanism of the depolymerisation of cellulose and on the primary steps in the formation of levoglycosan cannot be based on the composition of the distillation products. Yet Shafizadeh and Fu [12] have made the completely valid remark that electron spin resonance data showing the presence in the reaction medium of free radicals, which in the opinion of other workers [10,11] support a homolytic mechanism of rupture of glucosidic bonds in the thermal decomposition of cellulose, cannot provide direct evidence of the mechanism of bond rupture, since thermal depolymerisation may be accompanied by far-reaching decomposition by a radical mechanism.

The results of the comprehensive investigations on the complicated pyrolytic process involved in the thermal decomposition of cellulose support a radical–chain mechanism of the thermal depolymerisation of cellulose.

III. PRIMARY STEPS IN THE FORMATION OF LEVOGLYCOSAN IN THERMAL DECOMPOSITION

Hypotheses on the primary steps in the thermal depolymerisation of cellulose with the formation of levoglycosan cannot yet be confirmed experimentally. The usual methods of labelled atoms and deuterium exchange are inapplicable to cellulose, since no methods are yet available for introducing labelled hydrogen or oxygen into its molecule. Several possible schemes of primary reactions have been suggested, and are examined below.

Shafizadeh et al., on the assumption that rupture of a 1,4-polymeric (glucosidic) bond in cellulose is a consequence of intermolecular transglucosidation, consider that this reaction produces new terminal groups with unblocked 4-hydroxyls, which in turn may be involved in further transglucosidation on the continuation of the pyrolysis. Thus levoglycosan may be formed either directly from cellulose or via the intermediate formation of 1,2- or 1,4-anhydroglucopyranose (Fig. 2). The formation of 1,6-anhydroglucofuranose (in 3–4% yield) in addition to the main product—1,6-anhydroglucopyranose (yield 36%)—is regarded by these workers as direct proof of the intermediate formation of 1,4-anhydroglucopyranose, which may be converted into the 1,6-isomer. These workers assume that pyrolytic reactions can occur by various routes: 1,4-reaction does not exclude the direct involvement of 6-hydroxyls; formation of 1,2-anhydroglucopyranose is entirely possible, although thermal decomposition with formation of levoglycosan takes place when the 2-hydroxyl has been methylated just as in a control experiment without protection of this hydroxy-group [39]. The Reviewer regards the intermediate formation of 1,4-anhydroglucopyranose as improbable; this is supported by the failure of attempts to detect this compound among the distillation products from the thermal decomposition of cellulose. Special studies also showed that 1,4-anhydro-2,3,6-trimethylglucose was not the main product of the thermolysis of 2,3,6-trimethylcellulose. An earlier report [40] of the presence of 2,3,6-trimethylglucosan among hydrolysis products from the thermal decomposition of trimethylcellulose quite obviously does not prove the presence of 1,4-anhydroglucopyranose. This report [40] produced the objection by Shaw that, according to theoretical calculations, 1,4-anhydroglucopyranose cannot be

formed either as intermediate or as final product. Thus a mechanism of transglucosidation suggests that levoglycosan can be formed only directly via the 6-hydroxyl, by hydrogen transfer to the glucosidic oxygen, and only from amorphous segments of cellulose, in which the hydroxy-groups are not blocked by hydrogen bonds.

Gardiner [37] and Madorsky [41], who favoured the hypothesis that cleavage of a glucosidic bond occurred by a heterolytic mechanism, assumed that terminal units having a levoglycosan structure were formed via a 1,2-oxiran ring appearing with detachment of part of the cellulose molecule. However, this mechanism is inconsistent with the above features of depolymerisation, which show it to be a radical–chain process. Kilzer and Broido [42] assume that the thermal decomposition of cellulose is a chain process, with initial formation of an active oxygen anion in a terminal glucoside unit. The glucosidic 1-oxygen atom is replaced by the 4-oxygen of the same unit by an S_N2 type of reaction. The 1,4-anhydroglucopyranose formed as intermediate is then converted into either levoglucosan or 1,6-anhydroglucofuranose, while the active centre of the anion migrates to the next unit in the chain. However, this transition is impossible from steric considerations, since carbon atom (1) would be attacked on the side opposite to the primary hydroxy-group [35]. Furthermore, the formation of levoglycosan via 1,4-anhydroglucopyranose cannot be regarded as proved (see above).

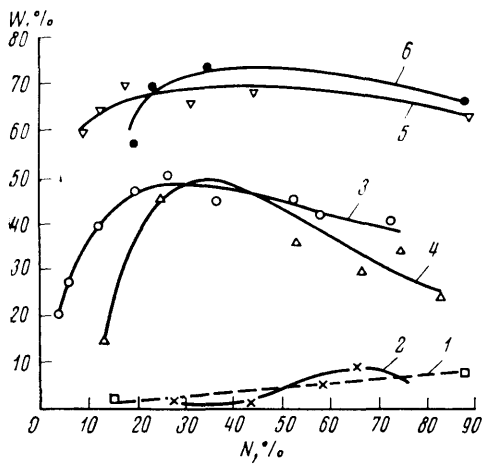

Figure 11. Effect of ash content on yield of levoglycosan W from the thermal decomposition of: 1) cotton cellulose (ash content 0.20%); 2) cellulose hydrate (0.20%); 3) cotton cellulose (0.05–0.09%); 4) cellulose hydrate (0.05–0.09); 6) cellulose hydrate (< 0.002%).

Investigators who favour a homolytic mechanism of rupture of the glucosidic bond suggest several possible ways in which levoglycosan may be formed, but these can be reduced to two main processes. Cleavage of the polymeric 1,4-bond may be followed by formation of an unsaturated bond at carbon atom (1) (radical I) at the 4-oxygen atom (radical II) (Fig. 10). The radical (I) formed at carbon (1) affects the stability of the 1,4-glucosidic bond of the next unit and causes it to break, after which the hydrogen atom migrates from the 6-hydroxy-group to carbon atom (4) with formation of a 1,6-anhydro-ring [7]. Formation of the alkoxy-radical (II) at carbon (4) of the monomer unit leads to intramolecular detachment of the hydrogen atom from the 6-hydroxyl and the appearance of a new alkoxy-radical [36,38]. The glucosidic link to the next unit is then attacked and broken by the alkoxy-radical, the free-radical centre is transferred to the next unit, and levoglycosan is formed at the same time.

The above sequence of primary steps in the formation of levoglycosan is shown in Fig. 10. One of these steps involves transition from the $C-1$ conformation to $1-C$. The formation of an uncompensated bond (a radical) in an acetal is a necessary precondition for a conformational change in the molecule. We can expect a similar effect if we regard cellulose as a polyacetal.

Kislitsyn [34–36] made a detailed examination of the mechanism of rupture of the glucosidic bond, and our analysis of his published experimental results supports the proposed scheme. However, doubt must be cast on his hypothesis that only one of the two macroradicals—the alkoxy-radical (II)—undergoes thermal depolymerisation with the formation of levoglycosan, while radical (I) undergoes far-reaching decomposition or is stabilised, since the yield of levoglycosan would not then exceed 50%, whereas yields up to 73% have been observed experimentally. Several workers [37,41–44] have given analogous schemes of rupture of a glucosidic bond differing only slightly from those considered above.

IV. EFFECT OF INORGANIC COMPONENTS ON CARBON–CARBON BOND RUPTURE AND DIRECTION OF THERMAL DECOMPOSITION

The influence of inorganic impurities on the yield of levoglycosan from the thermal decomposition of cellulose has been mentioned in a review [2]. Several papers [41,45,46] have referred to a diminished yield when inorganic salts are introduced into cellulose, but these investigations were not systematic. It therefore seems useful to consider here the effect of inorganic components on the rupture of a carbon–carbon bond and on the direction of the thermal decomposition of cellulose.

For a long time after Picter and Sarasin's paper [1] (1918) a high yield of levoglycosan could not be obtained, probably owing to insufficient information on the influence of inorganic components on the mechanism of the thermal decomposition of cellulose, and hence on the yield of levoglycosan. The marked difference in yields observed from cotton cellulose and from cellulose hydrate with ash contents respectively of 0.07% and 0.25% suggested [4,5] that not only the quantity of the mineral elements present but also their composition affected the direction of thermal decomposition. This hypothesis was supported by spectroscopic analysis of ash specimens from the two modifications, which showed that sodium salts changed abruptly the direction of thermal breakdown of cellulose hydrate: in the presence of 0.1–0.02% of sodium salts (reckoned as the mass ratio of sodium cation to cellulose) the process extends to products of far-reaching decomposition at carbon–carbon bonds: with < 0.007% of sodium, breakdown to levoglycosan becomes possible. The same workers then made systematic investigations on cotton cellulose and cellulose hydrate with ash contents of 0.2%, 0.05%, and < 0.002%. Fig. 11 shows that predominant formation of levoglycosan becomes possible with both modifications at an ash content of 0.09%, and is most complete with < 0.002% of ash.

Table 6 summarises the main results obtained [30,31] on the role of salt cations and anions. The average yield of levoglycosan from cellulose with initial spectroscopic contents of 0.03% of ash and 0.0003% of sodium is 48%, while the remaining 52% of products results from far-reaching breakdown. Introduction of chlorides of univalent metals (caesium, sodium, and potassium chlorides) as well as sodium thiocyanate produces a sharp decrease in yield of levoglycosan (to 0–1%) and an increase in the quantity of the latter products to almost 100% (experiments 2–5).

Table 6. Dependence of yields of levoglycosan W_l and of products W_s of the far-reaching decomposition of cotton cellulose on the salt content S (where R is the ionic radius, C the content of cations, and n the number of gram-atoms of cation per mole of cellulose unit).

Expt. No.	Salt	S, %	C, g-atom	n	R, Å	W_l, %*	W_f, %*
1	He added	0.03	—	—	—	48	52
2	CsCl	0.87	$4.6\cdot10^{-4}$	1.5	1.65	0	100
3	KCl	0.30	$3.6\cdot10^{-4}$	1.2	1.33	1–2	98–99
4	NaCl	0.30	$4.6\cdot10^{-4}$	1.5	0.98	1–2	98–98
5	NaCNS	0.42	$4.6\cdot10^{-4}$	1.5	0.98	1–2	98–89
6	LiCl	0.30	$6.2\cdot10^{-4}$	2.0	0.78	6.0	94
7	$BaCl_2$	1.07	$4.6\cdot10^{-4}$	1.5	1.43	9.0	91
8	$CaCl_2$	0.77	$4.6\cdot10^{-4}$	1.5	1.06	15.0	85
9	$ZnCl_2$	0.66	$4.4\cdot10^{-4}$	1.5	0.83	39.0	61
10	Cs_2SO_4	0.93	$4.7\cdot10^{-4}$	1.5	1.65	4.0	96
11	Na_2SO_4	0.30	$3.8\cdot10^{-4}$	1.3	0.98	12.0	88
12	$FeSO_4$	0.74	$4.2\cdot10^{-4}$	1.4	0.83	22.0	78
13	$ZnSO_4$	0.78	$4.2\cdot10^{-4}$	1.4	0.83	16.0	84
14	NaCl	0.04	$6.4\cdot10^{-5}$	0.2	0.98	10.0	90
15	NaCl	0.30	$4.6\cdot10^{-3}$	1.5	0.98	1.2	98–99
16	Na_2SO_4	0.05	$6.4\cdot10^{-5}$	0.2	0.98	22.0	78
17	Na_2SO_4	0.10	$1.3\cdot10^{-4}$	0.4	0.98	19.0	81
18	Na_2SO_4	0.30	$3.8\cdot10^{-4}$	1.3	0.98	12.0	88
19	Na_2SO_4	3.00	$3.7\cdot10^{-3}$	13.4	0.98	12.0	88
20	$ZnSO_4$	0.30	$1.6\cdot10^{-4}$	0.5	0.83	27.0	73
21	$ZnSO_4$	0.78	$4.2\cdot10^{-4}$	1.4	0.98	16.0	84
22	$(CH_3COO)_3Cr$	0.10	$3.3\cdot10^{-5}$	0.1	0.52	43.0	57
23	$(CH_3COO)_3Cr$	2.60	$1.0\cdot10^{-3}$	3.4	0.52	19.0	81

*Mean values from several parallel experiments.

These workers [30] then compared the influence of inorganic salts on the thermal decomposition of cellulose with the physical properties of the cation and the anion of the salt. They tried to establish whether the process was directly dependent on the stoichiometric proportions of salt cation and cellulose hydroxyls or whether it was catalytic. Calculation for the extreme salt contents of 0.05% and 3% showed that one cation corresponded to 2780 and 46.4 hydroxy-groups. Hence only a small proportion of the hydroxyls can be in direct contact with a salt cation; monomer units free from a cation should have decomposed with the formation of levoglycosan, which in fact does not occur. It was therefore assumed that the action of the salt was catalytic. Furthermore, calculation [30] of the ratio of the specific surfaces of salt and cellulose showed that the cellulose surface occupied by the salt was only around 2% of the total cellulose surface [30], which supports the hypothesis of a catalytic effect.

Thus the researches lead to the conclusions that inorganic salts contained in or introduced into cellulose promote thermal cleavage at carbon–carbon bonds with the formation of products of far-reaching decomposition. The nature of both cation and anion influences the direction of the thermal breakdown of cellulose.

V. USE OF RESULTS FOR PRACTICAL PURPOSES

Investigation of the directed thermal degradation of cellulose indicates [4–8,26] a low yield of levoglycosan at the first stage with both modifications, i.e. easily hydrolysable polysaccharides and monosaccharides.

The results made possible the development of a new combined method for processing plant material (instead of the hydrolytic process adopted at present) with the aim of obtaining monosaccharides as substrates for growing yeast and for other purposes. Industrially, a single, fairly narrow régime of hydrolysis (high temperature and pressure) is used to convert both readily and difficultly hydrolysable polysaccharides into monoses. Under the conditions adopted the monosaccharides break down, which leads to a loss of 30–40% of the carbohydrate components of the plant material.

At present there are no industrial methods for the combined processing of plant materials that, by organically coupling hydrolytic and pyrolytic processes, would permit the successive conversion of readily and difficultly hydrolysable polysaccharides and lignin of vegetable tissues into valuable chemical products. Study of the thermal degradation of cellulose in a high vacuum with external heating [7,23] yielded laws governing the direction of the process and a suggested mechanism for its thermal depolymerisation with the formation of levoglycosan. A high vacuum was necessary because of the low vapour pressure of levoglycosan, and a satisfactory yield could then be obtained by conducting the decomposition at a sufficiently low pressure; the same conditions also ensure maximum suppression of oxidising processes.

Comparison of results obtained by several workers showed [47] that increasing the residual pressure to 2–5 mmHg in reaction vessels with external heating produced a sharp drop in the yield of levoglycosan. This fact, together with the difficulty of ensuring uniform heating of large quantities of cellulose in the evacuated apparatus, made this method impracticable. For the first time, therefore, the directed thermal decomposition of cellulose was attempted [47] in a stream of superheated steam or an inert gas at a low pressure and preheated to a temperature below that required for the decomposition. This enabled (i) air to be displaced from the reaction vessel independently of the residual pressure, thereby preventing oxidising processes; (ii) direct contact to be established between the heat-transfer agent and any quantity of material, so that heating was more uniform; and (iii) the heat-transfer agent to be used to accelerate exhaustion of the decomposition products from the high-temperature zone. This method has since been applied successfully on laboratory and pilot-plant scales.

Researches undertaken by a group of workers [48–50] laid the foundations of a new technology for the combined processing of vegetable materials in which hydrolytic processes are used only to convert readily hydrolysable polysaccharides into monosaccharides or furaldehyde, while difficultly hydrolysable polysaccharides and lignin are converted into several valuable products by the thermal decomposition of cellulose and lignin in a single technical cycle. The total yield of products is 78% in the combined method, instead of 30–40% in the modern hydrolytic industry. Results of this work were shown at the VDNKh "Science 1967" Exhibition and at the "Chemistry 70" International Exhibition.

Thus the coupling of hydrolytic and thermal processes enables vegetable material to be processed with more efficient utilisation of its components and also yields

products that can be exploited in various branches of the national economy. This method achieves degradation of cellulose to a monomer (levoglycosan) and the thermolysis of lignin in a single industrial cycle. A carbonaceous residue remains (10–15%).

The furaldehyde and the monosaccharide formed in the combined method are used on existing lines. The tar from the vacuum thermolysis (the water-insoluble part) can be employed for the preparation of tanning agents, foundry binding agents, etc. The carbonaceous residue (Karbost) has been tested as a substitute for difficultly available materials—Megrozin, sawdust, lampblack.

Since levoglycosan might become a commercial product for the first time, and experience of its application is lacking, both abroad and in the Soviet Union, research was undertaken on possible uses for it and its derivatives, and on developing methods for preparing some of them. Research on the application of levoglycosan is the subject of a separate paper. Only certain possibilities will be mentioned below. It may find application as a monomer for synthesising the polymer dextran[51,52]. Copolymers of the methacrylic ester of levoglycosan have been claimed[53] in the production of artificial membranes with carbohydrate residues in medicine. Levoglycosan can yield pigments used in the manufacture of daylight-fluorescent paints and enamels[54]. Chemically pure levoglycosan can be employed as a substitute for pharmacopoeial glucose in the tableting of medicinal preparations.

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Rheological Properties of Thermosetting Compositions

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The current state of research on the plastic properties of compositions based on reactive oligomers is assessed. Methods used to study their properties during deformation are examined. The influence of external factors, composition, and specific structural features of the compositions on their residence time in the plastic state and on their deformation characteristics is discussed. Possible lines of investigation on the rheological properties of thermosetting compositions are considered. A list of 135 references is included.

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I. INTRODUCTION

Thermosetting compositions are based on reactive oligomers and fillers, plus any required additives. The distinguishing feature of these materials is their inherent ability, when heated or at a low temperature, to pass into an infusible and insoluble state by the formation of steric bonds (a three-dimensional network) as a result of chemical reactions[1-4]. Thermosetting resins, in contrast to many thermo plastics, are highly resistant to arcing and possess good dielectric properties; they are stable in many corrosive media and exhibit considerable rigidity. Because of this combination of valuable properties thermosetting plastics find diverse applications in the national economy[5].

The character of the reactions which cause the setting of reactive oligomers largely determines the conditions of formation of high polymers, and hence should be taken into account in the choice of technical scheme for the processing of oligomeric substances into a polymeric material. Reactive oligomers can be divided[6] into several groups: (1) those having multiple bonds and cyclic oligomers, able to undergo chain and stepwise polymerisation — "polymerisation oligomers" —including oligoester-acrylates, oligosiloxanes, polymers and copolymers of butadiene and isoprene, etc.; (2) oligomers containing functional groups are able to undergo polycondensation, migration copolymerisation, or polycoordination — "oligomers with functional groups" (phenol-formaldehyde, urea, glyptal, etc.); and (3) oligomers having a chain of π-conjugation which may contain functional groups, including oligovinylenes, oligophenylenes, etc.

In the present Review we shall consider mainly materials of the second type. Actual cross-linked polymers are characterised by various structural inhomogeneities, which explains in particular their diminished strength (in comparison with the calculated value), as well as the ability to flow at high temperatures and pressures possessed by certain irregular polymers with a low density of cross-linking.

Structural inhomogeneity affects not only the mechanical and physical properties of the material but also the kinetics of further cross-linking, which may involve both groups attached to the existing three-dimensional structure and those located at more accessible sites. It may therefore be expected that the same primary reaction, especially at relatively high degrees of conversion, will exhibit different rate constants, representing different kinetic mobilities of the units of the three-dimensional structure.

The properties of polymers may vary within wide limits depending on the structure, chemical nature, and frequency of cross-links[6] Polymers possessing neither solubility nor the capacity of viscous flow are formed only on the attainment of quite high degrees of conversion of the initial multifunctional compounds. The formation of three-dimensional cross-linked polymers is accompanied by a gradual loss of fluidity and concomitant increase in viscosity. It is therefore important to assess the rheological properties of the system in order to elucidate the nature of the processes occurring in reactive oligomers and filled compositions based on them.

Three types of processes — direct extrusion, transfer moulding, and injection moulding with preliminary mastication of the material —are now widely employed for converting thermosetting compositions into finished articles[7].

Many publications on the processing of thermosetting resins usually point out the need to establish high injection pressures[8-10]. Materials based on phenol-formaldehyde oligomers can be processed properly with almost all types of equipment, including moulding machines with worm mastication. The considerable heat resistance of materials based on reactive oligomers enables them to be processed in ordinary extruders[11-14].

The difficulty of processing lies in the near impossibility of drawing a boundary between the end of mastication and the beginning of setting, since irreversible cross-linking begins to develop at the same time as softening of the material[15]. No significant part is played by the particle size of the thermosetting compositions when the material is fed into the channel of the worm. However, the friability of the mass to be processed is significant[9].

Pressure is another important variable in processing. The permissible pressure is lower for materials that tend to undergo mechanical degradation and disintegration at high rates of processing. Thus aminoplasts are processed at only half the rates of deformation used with phenoplasts[16]. The maximum rate of injection can be realised in the processing of phenol-formaldehyde compositions and materials based on melamine-formaldehyde oligomers.

High pressures and rates of injection of thermosetting melts cause intense wear of moulds and gates, but in some

cases this is attributed to inadequate mastication of the material[16]. This is probably responsible also for the vigorous evolution of heat when an attempt is made to increase the capacity of the machine by rotating the worm more rapidly. Few if any data are available on the homogeneity of the melt in the channel of the worm. Estimation of this property from the extruded material emerging from the die is unreliable, since intense mixing may occur during extrusion, as in the processing of elastomers and thermoplasts. It has been suggested[17] that the quality of mastication can be assessed in several cases e.g. from the temperature of the material leaving the masticator.

This optimisation of the processing of thermosetting compositions requires an investigation of the change in their properties on passing from initial to plastic and then to hardened state, i.e. the rate of passing from one state to another, the duration of the plastic state. It is also necessary to study the effects of numerous technical factors—temperature, speed, pressure, degree of filling, and particle size of filler—at all stages of processing.

II. ASSESSMENT OF PLASTIC PROPERTIES OF THERMOSETTING COMPOSITIONS BY RHEOLOGICAL METHODS

The maximum amount of information on the state of the material and the role of various factors in its processing can be obtained by making rheological measurements under conditions approximating to actual moulding.

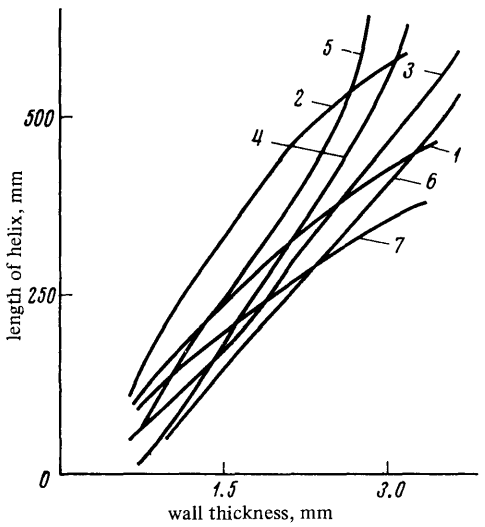

Figure 1. Comparison of fluidities of phenoplasts and various thermoplastics with longitudinal filling of a helical cavity (injection pressure 700 kg cm^{-2}): *1*) Genal 4000 phenoplast; *2*) Genal 4050 phenoplast; *3*) polypropylene; *4*) glass-filled nylon; *5*) polystyrene: *6*) ABS; *7*) Genal 4300 phenoplast.

The standards required for the composition to be processed are increasing because of the great sensitivity of injection moulding to variations in the properties of the material; in particular, the scatter of material characteristics from batch to batch must be as small as possible. It is also desirable to lengthen the time the material remains in a plastic state, and to diminish the viscosity of thermosetting compositions. A single system for assessing the viscosity properties of the latter is lacking, because of the poor reproducibility of measurements made with different designs of apparatus[18].

The principal characteristics which must be used to compare thermosetting compositions are the initial viscosity, the time the material remains in a plastic state, the duration of setting, and the change in fluidity during setting. The initial viscosity and the duration of the transition from plastic to hardened state are often determined at a standard temperature[18]. It is noteworthy that thermosetting compositions in a plastic state approach melts of ordinary thermoplastics in their viscosity characteristics (Fig. 1).[19]

The most diverse methods are used for determining those technical characteristics of thermosetting compositions that may be useful under practical conditions, but systematic accounts of them can be found[20,21]. The first group involves estimating fluidity during extrusion, when the results depend on the conditions of deformation. In the second group of methods the viscosity is determined under conditions approximating to those of injection moulding and extrusion.

Among the numerous methods of the first group the most widely used are the examination of fluidity by compression between two plane-parallel plates[22], the "beaker method"[23,24], extrusion through different channels[25–29] and its *Rossi-Peaks* modification, determination of fluidity during flow into a conical channel[31] or into a mould in the form of an Archimedean screw[24,32,33], etc.[34–36]. All these methods involve obtaining arbitrary characteristics, which does not permit adequate assessment of the fluidity of thermosetting compositions.

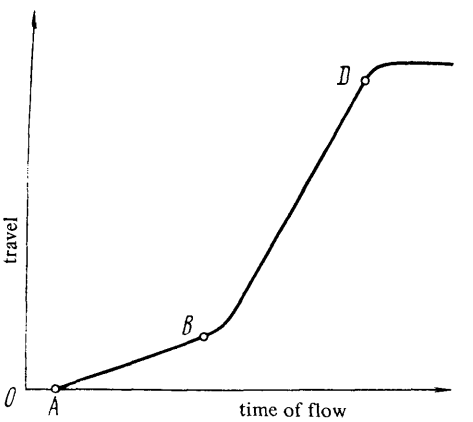

Figure 2. Assessment of viscosity properties of thermosetting compositions by Meysenbug's method (Darmstadt test): *OA*) heating range; *AB*) softening range; *BD*) flow range; *D*) start of setting of composition.

The second group of methods are based mainly on rotary viscosimetry, which enables the experimental conditions (temperature, duration, régime of deformation) to be varied within very wide limits[37–46]. Those most widely used for thermosetting compositions are Meysenbug's method[47,48],

the flow test[49,50], the Kanavets apparatus[51–55], and the Brabender plastograph[49,56–59]. The test results are used to determine the duration of the plastic state, the viscosity properties of the material, the rate of setting, etc.[60]. Figs. 2[20] and 3[61] illustrate typical relations. The methods differ in the mode of deformation, either specifying a constant torque and recording the variation in rate of flow with time, or using a specified constant rate of travel and measuring the resulting torque.

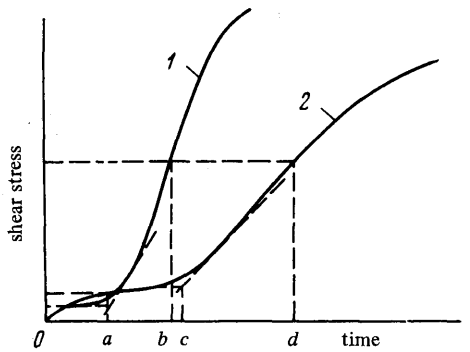

Figure 3. Kinetics of the hardening recorded on a Kanavets plastometer[35] of thermosetting materials of: *1*) Novolak type; *2*) resol type; *Oa*, *Oc*) periods of time in plastic state; *Ob*, *Od*) setting times.

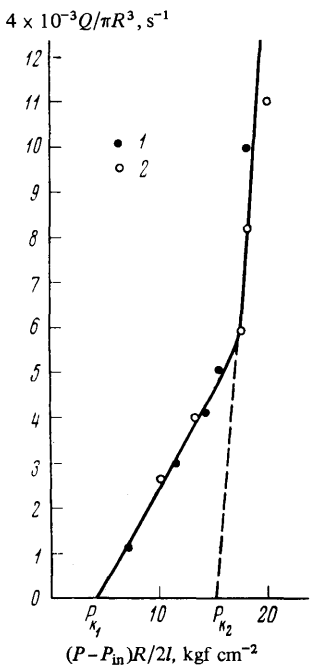

Figure 4. Flow curve of K-18-2 composition: P_{k_1}) lower fluidity limit; P_{k_2}) upper fluidity limit; R) radius of gate; *1*) 1 mm; *2*) 1.5 mm; Q) bulk flow rate; l) length of gate; $P-P_{in}$) pressure drop in channel.

Knowledge of the rheological properties of the compositions under processing conditions is necessary in order to compare the mouldability of different thermosetting materials and describe the flow of the melt in the pouring channels and the mould cavity[62–65]. Capillary and capillary–rotary instruments are also used[66]. Rheological properties were determined[62] by extruding the material through gates of different diameters, the main result being the discovery of two fluidity limits for a composition (Fig. 4). The flow curves were described analytically by means of Bingham's law. Capillary viscosimetry yielded[67,68] flow curves for a composition analogous to the Soviet material K-18-2 at shear stresses not exceeding 5 kg cm^{-2}, below the lower fluidity limit P_{k_1} (Fig. 4). The flow curve was satisfactorily described[67] by a power relation of the type

$$\tau = k \cdot \left(\frac{4Q}{\pi R^3}\right)^{\frac{1}{n_1}},$$

where τ is the shear stress, Q the space velocity, and R the radius of the capillary, while the constants were k = = 1.0 (kg cm^{-2})^{n_1} s and n_1 = 2.07. However, both here and in other work[37,68,69] capillary flow curves were obtained only at one temperature. Hence the results do not permit calculation of the activation energy of deformation, which would have permitted a fuller comparison of the technical properties of the compositions.

Use of a PPR-1 rotary instrument to examine the rheological properties of K-18-2 composition with deformation at a constant rate of shear revealed a limiting shear strength, which rose with increase in the intensity of deformation[70]. However, no limiting stresses like the Bingham fluidity limit were detected[70], in contrast to earlier statements[62,66]. A limiting shearing strength is typical[71–73] of the breakdown of the three-dimensional structural framework formed by the disperse phase (sawdust). Plastic disperse systems, among which thermosetting melts may be included, exhibit a fall in shear stress with increase in rate of deformation on passing through the limiting shearing strength.

Investigation of the rheological properties of K-18-2 moulding powder on a Brabender plastograph revealed[43] considerable boundary-layer slippage during movement of the mass in the gap between the working members. However, another worker[68] observed no slippage of material in the boundary region.

Thus results of the above work on the viscosity properties of thermosetting materials by capillary and rotary viscosimetry have occasionally been contradictory.

Dynamic methods are currently in widespread use for investigating the most diverse materials. Information obtained in this way enables us not only to determine the temperature of transition from one state to another but also to record the development of particular processes with time. The use of dynamic methods also avoids breakdown of the structure, like that occurring during deformation in rotary and capillary viscosimeters.

Despite the promise of the dynamic method, very few results have been obtained on thermosetting compositions, although the first attempts have been made to determine the duration of the plastic state of the binder at various temperatures. Thus the setting of phenolic oligomers and unsaturated oligoesters has been investigated[74] by means of a torsional pendulum, and a similar determination has been made[75] of the viscoelastic properties of the binder. Somewhat apart from these investigations are experiments on the viscoelastic properties of oil-filled phenolic oligomers near their glass point[76]. By varying the oil content

from 0 to 50% the temperature dependence of the mechanical loss angle tan δ was obtained for four frequencies. The results indicated the relation

$$T_g = A \cdot \lg \varphi + B$$

between the degree of cross-linking φ and the glass point of the oligomer T_g, where A and B are constants. The molecular mobility of the phenolic oligomer is assumed to be independent of the degree of cross-linking.

III. EFFECTS ACCOMPANYING THE DEFORMATION OF COMPOSITIONS BASED ON REACTIVE OLIGOMERS

Results obtained by the above methods are sometimes used to plot relations between shear stress and rate, (flow curves), as in the investigation of the viscosity properties of thermoplastics and elastomers. However, most workers do not regard this as possible, probably because it is not generally accepted that viscous flow can take place in thermosetting compositions. Indeed, until recently no studies had been made of their viscosity properties at low rates of shear by means of various rotary instruments, nor had the constancy of the flow curves been verified when compositions were extruded through capillaries of different radii.

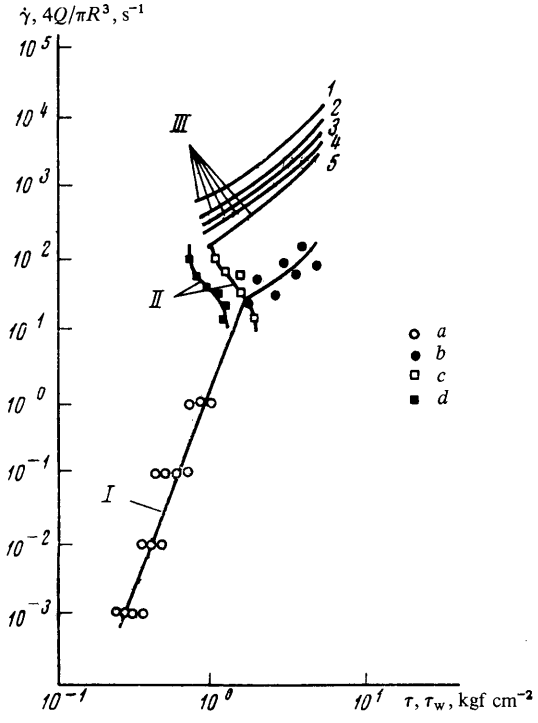

Figure 5. Flow curves of K-18-2 compositions without a hardener at 120°C: I) region of flow (viscosimeter: *a*) REV-1; *b*) capillary); II) pressure dependence of bulk flow rate measured with cylinder–cylinder type of viscosimeter (surfaces of working members: *c*) grooved; *d*) smooth); III) dependence of $4Q/\pi R^3$ on τ_w obtained with capillary viscosimeter [diameters of capillaries (1–5 mm) indicated on curves].

Boundary-layer slippage plays a decisive role[77,78] over wide ranges of shear stress and rate of shear (at rates of deformation of phenoplasts closely similar to those of actual processing conditions). External friction between the material and the wall of the channel may lead to a sharp increase in rate of rotation of the worm. Similar results are obtained in the deformation of thermoplastics[79], for which it has been shown in particular that the rate of slippage is independent of temperature. Region (II) in Fig. 5,[77] in which the shear stress falls with increase in rate, is especially interesting. In the case of raw rubbers this phenomenon was at one time attributed to breakdown of the structure[80,81]. In this case slippage of the material relative to the measuring surfaces is possible[79,82], and the same conclusion was reached by the above workers[77,78].

However, a decrease in stress with increase in rate cannot always be detected in the tests. Thus with elastomers the transition from internal to external friction during extrusion through a capillary takes place at constant stress while the rate increases several dozen times[83]. An analogous phenomenon has been recorded in the investigation of thermosetting compositions, although it was explained by the development of degradation[84].

A characteristic sign of the development of rubberlike elasticity in a polymeric material during extrusion through a capillary is the swelling of the jet of extrudate. Since thermosetting compositions are based on reactive oligomers with different degrees of filling, strongly developed rubberlike elasticity is hardly to be expected. This is supported by results obtained with phenolic compositions[85] which showed that the mould was filled by a molten jet equal in diameter to the gate, this work also indicated that binder and filler may separate, which would impair the homogeneity and the strength characteristics of the final article[85]. This effect was due not only to poor adhesion between binder and filler but also to inadequate homogenisation during mastication. An experiment was therefore undertaken in which the extrudate emerging from the nozzle was divided into four parts, the fluidity of each of which was determined by a standard method. The pouring properties deteriorated along the extrudate, which confirmed the hypothesis that the initial composition had been insufficiently homogeneous.

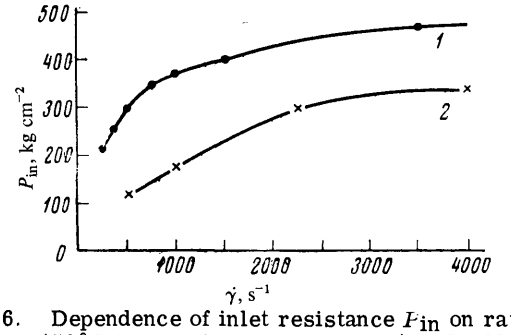

Figure 6. Dependence of inlet resistance P_{in} on rate of shear $\dot{\gamma}$ at 150°C for moulding material: *1*) K-21-22; *2*) K-214-2.

A specific problem in the processing of thermosetting compositions is the need to establish considerable pressures in the dispensing zone, owing to the great pressure losses on entry to the gate. This hypothesis is supported

by the experimental results[63,77,86] plotted in Figs. 6 and 7. Such considerable pressure losses might apparently be due to the development of cross-linking, but the same results are observed in the absence of a hardening agent[77] as in its presence[63,86]. The need to establish high pressures is probably due to the high viscosity and considerable limiting shear strength of thermosetting compositions with finite degrees of filling. The pressure in the dispensing zone can be somewaht lowered if the geometry of the inlet is modified. Thus by changing the inlet angle by 60° we can not only eliminate stagnant zones but also reduce the input losses on the average by 25%.[87]

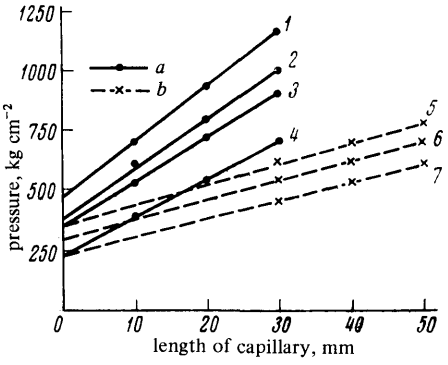

Figure 7. Dependence of pressure on length of capillary for the flow of K-21-22 moulding material at 150°C through an orifice of diameter: *a*) 2 mm; *b*) 4 mm with different rates of shear (s^{-1}): *1*) 3500–3800; *2*) 1400 to 1500; *3*) 950–1000; *4*) 330–360; *5*) 720; *6*) 480; *7*) 200 to 300.

Examination of the fluidity of moulding materials by Meysenbug's method showed[88] that adding up to 1% of a plasticiser considerably improves the reproducibility of estimates of the properties of the compositions. However, the fluidity remains almost unchanged with variation in the plasticiser content from 1% to 3%. The reproducibility of the properties of thermosetting compositions in quite convincing evidence of the favourable effect of the plasticiser[89]. It is interesting that plasticisers that do not react chemically with the oligomer enhance the plasticity of the composition at all stages while hardly affecting the duration of the plastic state[90]. However, if chemical reaction occurs between plasticiser and oligomer, not only a decrease in viscosity but also a longer period in the plastic state is observed.

An attempt was made[62,63] to use the measured coefficients of friction of the test materials to calculate the loss of pressure at the inlet to the nozzle. Thus for K-21-22 material with a rate of shear of 500 s^{-1} the pressure difference at the inlet to the channel found by Bagley's method[91] was 300 kg cm^{-2}, while the pressure loss due to friction of the thermosetting composition was 90 kg cm^{-2}. The difference between these values was then taken in the viscosity calculations to be the pressure loss at the inlet to the die. These workers considered that slippage of material relative to the walls of the capillary was almost completely absent in the deformation of thermosetting compositions at such considerable rates of shear. Their results enabled the input correction P_{in} to be related to the rate of shear $\dot{\gamma}$ by the power formula

$$P_{in} = C \cdot \dot{\gamma}^a,$$

in which C and a are constants depending on the properties of the moulding materials and the temperature[63]. A formally similar relation was obtained[77] with the rate of slippage as variable, when the input correction was unaffected by temperature.

Study of the rheological properties of thermosetting compositions shows that careful reproduction of the test conditions is necessary for the results to be comparable. Plastometers with parallel plates and rotary viscosimeters are therefore becoming ever more widely used. A comparison was made[58] between results obtained with a Brabender plastograph using an extruder as mixer and those obtained with a Kanavets type of rotary viscosimeter. Experiments with a phenol–cresol–formaldehyde oligometer filled with sawdust are noteworthy[58]. With 5 g of material at 100°C and the rotor rotating at 30 rev/min almost complete irreproducibility was found, since the test mass stuck to the mixer paddles and the drag fell sharply. Analogous disintegration of the specimen can occur also in tests with rotary instruments of the cone–plane type, in which hydrostatic pressure is absent. As a consequence, the dependence of rate on torque may acquire the form described by other workers[77,78,80–82].

It is of the greatest interest in investigating the rheological properties of thermosetting compositions to establish flow in a capillary, since conditions then approach those of actual injection moulding. The need for high pressures, the almost complete absence of rubberlike elasticity after emergence from the capillary, and also the rheological results indicate the "rodlike" motion of the compositions[77]. The experimental results show that the rate of discharge is almost entirely determined not by flow but by the rate of boundary-layer slippage v_0. The dependence of stress τ on this rate is then[77]

$$\tau = A_s \cdot v_0^m,$$

where A_S and m are constants. Measurements for technical purposes can be speeded up by using a capillary viscosimeter[93] with automatic recording of the relation between stress and rate of deformation. Deformation conditions accompanying slippage and calculations of the chief parameters (stress and rate of shear, rates of slippage) have been discussed in detail[94–100].

Investigation of the flow at low rates of deformation of compositions based on reactive oligomers has shown[101–106] that the rheological properties of the oligomers—Newtonian liquids—change abruptly when fillers are added to them. At a certain filler content a régime of boundary-layer slippage is established when the compositions undergo deformation in capillary and in rotary viscosimeters.

IV. EFFECT OF TECHNICAL MOULDING CONDITIONS ON PROPERTIES OF THERMOSETTING COMPOSITIONS IN THE PLASTIC STATE

In order to investigate the viscosity properties of thermosetting compositions under conditions as close as possible to actual processing schedules, a Kanavets type of plastometer was fixed to the outlet from the masticator nozzle, enabling the viscosity of the material to be determined at a rate of shear of 0.014 s^{-1}, low enough for the effect of the heat produced by friction to be neglected[107].

Application of relations used[40,61,108] to describe the behaviour of thermosetting materials showed that the temperature in the masticator should not exceed 120°C when standard compositions were processed: otherwise premature setting takes place[109]. Fig. 8 illustrates the temperature dependence of the time during which the material remains in a plastic state[107].

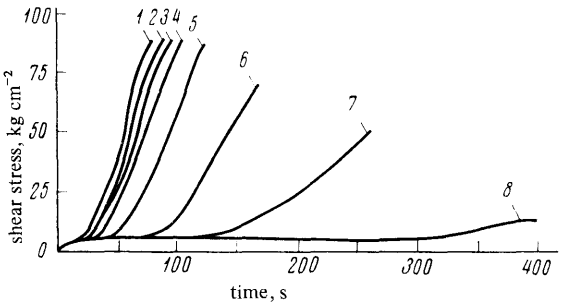

Figure 8. Kinetics of the setting of a phenol–formaldehyde composition at different temperatures (°C): *1*) 190; *2*) 180; *3*) 170; *4*) 160; *5*) 150; *6*) 140; *7*) 130; *8*) 120.

The physicochemical properties of articles made from thermosetting compositions exhibit anisotropy owing to orientation of the filler particles[85,107,110]. Orientation of the oligomer itself during injection moulding probably makes no contribution[85]. At some distance from the gate filler particles are usually oriented perpendicular to the direction of flow; in narrow channels the orientation is parallel. The orientation effect is diminished by under extrusion: i.e. injection takes place into an open mould; parts which initially break off under the influence of pressure, then join with great force[32].

The use of high pressures in the processing of thermosetting compositions naturally raises the question of the effect of pressure on their fluidity and on the duration of the plastic state. Results obtained[31] by the methods of Schwittmann and of Meysenbug were quite reproducible, but were not compared with those obtained by other methods. Work on melamine and phenolic oligomers showing that the duration of the plastic state becomes shorter with increase in pressure[88] is of greater interest. A study of flow during extrusion[64] revealed direct proportionality between rate of flow and pressure up to around 600 kg cm^{-2}, which suggested that Newtonian flow was maintained up to high pressures. However, no more data have appeared on the Newtonian flow of a filled composition, despite the numerous investigations in this field made with various types of viscosimeters[37,43,62,63,66–70,77,78,111–114].

In the "beaker" method it was suggested[64] that pressure, viscosity η, and dimensions of a standard "beaker" were interrelated by the formula

$$\frac{\bar{p}}{\eta\bar{\omega}H} \approx 0{,}5\left(\frac{R}{d}\right)^2,$$

where d is the thickness of the wall of the vessel, H the depth of the specimen, and $\bar{\omega}$ the mean speed of the plunger, while $\bar{p} = \pi R^2 \Delta\bar{p}$, in which $\Delta\bar{p}$ is the mean extrusion pressure.

The fluidity of a composition not only varies on passing from one type of oligomer to another but also is largely dependent on the moisture content of the initial material[115,116]. Usually the latter does not exceed a few percent, since further increase, in spite of the consequent decrease in viscosity, produces a sharp deterioration in physicomechanical properties of the hardened composition.

The particle size of the filler has a noteable effect on the viscosity properties of the thermosetting composition: it was shown for the typical compositions K-18-2, K-21-22, and others that increase in the particle size from 0.1 to 0.5–0.6 mm not only increases the viscosity of the system but also considerably shortens the period in a plastic state[117]. Unfortunately, very few data have been published on the effect of the filler content on the rheological properties of thermosetting materials[101–106].

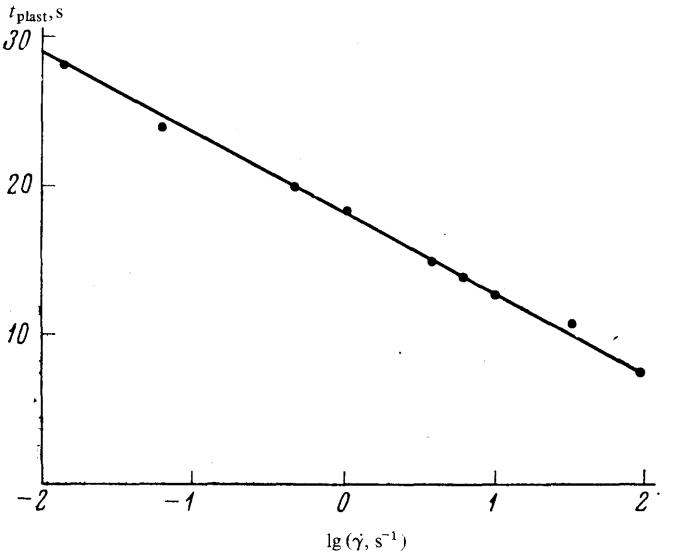

Figure 9. Dependence of length of stay of K-18-2 in plastic state t_{plast} on rate of deformation $\dot{\gamma}$ at 170°C.

This latter omission is aggravated by the impossibility of transferring to thermosetting materials methods of calculating deformation régimes developed for thermoplastics[71,72], because of their specific character. In moulding machines with worm mastication the former materials are processed at very high rates of deformation. Analogous conditions in the processing of thermoplastics may cause the polymer to crystallise[118,119] or to break down[120–122]. Intense deformation also intensifies chemical reactions[78], which is of especial interest for the processing of thermosetting materials. Fig. 9 shows that the time in the plastic state becomes shorter with increase in rate of deformation[41,123]. The role of deformation in the setting of a composition is largely determined by the temperature: e.g. deformation at 120°C may shorten the period in the plastic state by factors of about 4–5, whereas at 170°C by factors of only 2–3 for the same range of shear rates. These conclusions are supported by the results of capillary viscosimetry[37]. The preliminary rolling of thermosetting

compositions also shortens the period the material remains in a plastic state.

The kinetics of setting— the second most important process occurring during the moulding of articles from thermosetting compositions— is mostly assessed by a rheological method[40,61] which has found widespread use both in the Soviet Union and abroad. However, several other methods are known for studying the hardening process, based on the measurement of physicomechanical, electrical, and thermal characteristics of the material, as well as chemical methods. Thus rates of setting have been determined by a thermochemical method[124], from the volume shrinkage[125,126], the variation in molecular weight[127], the variation in dielectric properties[128], chromatographically[129,130], by infrared spectroscopy[131], from the proportion of acetone-insoluble oligomer[132], etc.[111]. The quantity of ammonia evolved has been used[133,134] to study the kinetics of the hardening by hexamethylenediamine of the phenol-formaldehyde oligomer No. 18 and the composition K-18-2 based on it.

Many different theories have been suggested to account for the rheological behaviour of elastomers and thermoplastics during deformation. No mathematical model which would describe the behaviour of thermosetting compositions during deformation is yet available, despite our knowledge of the variation in their properties with various factors and the accumulation of much experimental information. We shall therefore consider only an attempt[135] to describe the flow of a thermosetting material in a cylindrical mould. This started from the pressure dependence of the bulk flow rate Q

$$a_n \frac{d^n Q}{d p^n} + a_{n-1} \frac{d^{n-1} Q}{d p^{n-1}} + \ldots + a_0 Q = Q_0, \qquad (1)$$

and was confined to the simplest cases with $n = 1$ and $n = 2$. The constants $a_1, a_2, \ldots, a_n$ depend on the properties of the material undergoing processing and on the conditions of filling of the mould, while Q_0 is the volume of the casting. With the boundary conditions $p = 0$ when $Q = 0$ and $p \to \infty$ when $dQ/dp = 0$, the relation

$$Q = Q_0 (1 - e^{-\frac{p}{r}}) \qquad (2)$$

was obtained for $n = 1$. The constant r depends on the length l and cross-section S of the die, the duration of flow t_v, and the effective viscosity of the composition η^*:

$$r = r(l, S, t_v, \eta^*).$$

This dependence was written

$$r = (l \sqrt{S})^{\alpha} \frac{\eta^*}{t_v},$$

in which α is constant for the apparatus used. Solving the differential equation (1) for $n = 2$ yields

$$Q = Q_0 + C_1 e^{-\frac{p}{r_1}} + C_2 e^{-\frac{p}{r_2}}, \qquad (3)$$

where r_1 and r_2 depend on the properties of the composition and the conditions of filling of the channel, while C_1 and C_2 are integration constants. The value of r was found from the slope of the plot of $\ln (Q_0 - Q)$ against p. The results[135] indicate that the deformation of polymerisation oligomers is well described by formula (2), and that of polycondensation oligomers by formula (3).

In view of the above results of investigations on the deformation of thermosetting compositions, in which the rate of slippage predominates (under conditions approximating closely to actual processing), it is necessary to set up a mathematical model of the injection moulding of these materials allowing for the "rodlike" character of their motion in channels, and also to develop a rheological model to describe the flow of materials based on reactive oligomers.

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Applications of Heteroligand Complexes in the Analytical Chemistry of Niobium and Tantalum

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Modern precision spectrophotometric and extraction-spectrophotometric methods for the determination of niobium and tantalum are based on the use of heteroligand (ternary, quaternary, and mixed) complexes of these elements with organic reagents. These methods make it possible to determine niobium and tantalum in complex materials without separating the components, which has greatly extended the scope of analytical methods in the chemistry of niobium and tantalum. The bibliography includes 131 references.

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I. INTRODUCTION

Inorganic chemical analysis has been developing recently in two main directions. On the one hand, much attention has been devoted to problems of specific synthesis of organic reagents used in spectrophotometric, extraction-photometric, chromatographic, and other analytical methods to ensure their greater specificity and sensitivity in relation to inorganic ions. The second trend is associated with more extensive use in inorganic analysis of ternary, quaternary, and multicomponent (mixed) chemical complexes, which are also referred to as heteroligand complexes. In mixed complexes containing different types of groups, the individual characteristics of the elements are manifested more clearly, namely their capacity for coordination (which is not quite so clearly shown in homoligand complexes), the stabilisation of unstable valence states, and the creation of more favourable conditions for transitions from one valence state to another. The use of reactions involving the formation of heteroligand complexes in spectrophotometric analysis has greatly extended the scope of the methods for the determination of many elements, including niobium and tantalum.

The chemistry of heteroligand complexes has been developed in relation to analytical chemistry in studies by Babko[1,2], Alimarin[3], Pilipenko[4], and others. The applications of heteroligand complexes have been reviewed in detail[1-5].

The use of organic reagents has greatly extended the scope of the spectrophotometric analysis of inorganic ions. During the first period, mainly two-component systems

were investigated, while problems of sensitivity and selectivity associated with the employment of metal ion–organic reagent systems were still not adequately solved.

The sensitivity of photometric reactions, expressed by the molar extinction coefficient ϵ, is greatly influenced by the stability of the chelates formed. The maximum value of ϵ can be estimated theoretically [6] as $\epsilon_{max} = 1 \times 10^5$. However, this sensitivity is provided by only a few reagents. To increase the sensitivity, new chromophoric groups are introduced into the organic reagents, using complexing agents which are as selective as possible; it is necessary that the spectrum of the resulting two-component complex should differ markedly from that of the initial reagent. The choice of selective reagents is also difficult because certain metal ions (niobium and tantalum, zirconium and hafnium, molybdenum and tungsten, etc.) have very similar electronic structures, ionic radii, and ionic potentials. An enhanced selectivity can be achieved by changing the ligand, by introducing substituents, and by altering the distances of the electron-donating groups within the molecule. Selectivity in an analytical reaction can be appreciably improved by masking, but this too has its limits, since the analytical reagent can react also with the masked ion.

A great increase of sensitivity and selectivity can be achieved with the aid of heteroligand complexes, using their optical properties. Mention should first be made of ternary complexes, although recently a number of reports have been published on the applications of quaternary complexes in spectrophotometric analysis [7,8].

In many cases (particularly for heavy metals with high valences) the mechanism of complex formation in the interaction of a two-component system MX with a new ligand Y is not based on competitive relations, i.e. on the displacement of one of the previous components by a third component, and the interaction in the system is more complex than the process

$$MX + Y \rightleftarrows MY + X. \qquad (1)$$

The new ligand enters into the composition of the coordination sphere, forming a heteroligand complex:

$$M^{z+} + mH_aX + nH_bY \rightleftarrows [MX_mY_n]^{z-am-bn} + [am + bn]H^+... \qquad (2)$$

The formation of the heteroligand complex is a fairly complicated process. The new ligand can form an associated ionic species with the initial homoligand complex; it can displace water molecules from the coordination sphere, although in principle complexes such as $M(H_2O)_nX_m$ and MH_nX_m belong to the group of heteroligand complexes themselves. In many cases heteroligand complexes are also formed in extraction processes.

Complexes with different metals, obtained in accordance with the equation

$$pM^{z+} + qM'^{u+} + H_aX \rightleftarrows (M_pM'_qX)^{pz+qu-a} + aH^+, \qquad (3)$$

are less important in analytical chemistry, because in practice one employs an excess of the ligands and the formation of such complexes is suppressed. One can quote only a few examples of their employment in analytical practice: (a) indirect polarographic determination of zirconium as zirconium lead tartrate [9] and photometric determination of cadmium as cadmium iron tartrate [10]; (b) the tin–iron–dimethylglyoxime system has been investigated by Babko and Mikhel'son in relation to analytical chemistry [11,12]; the complex has been used by Elinson and Tsvetkova [13] to develop a method for the determination of tin in alloys with zirconium and niobium; (c) the formation of complexes of the type $M_pM'_qX$ can explain the extraction of metal ions by two other metal ions, which has been observed by Alimarin and Gibalo [14].

Coordination compounds formed in accordance with Eqn.(2) by one metal with two or several ligands are particularly important. It has been shown in a number of studies that the electrostatic interaction in the complex and the ligand effect promote the formation of a heteroligand complex. Electrostatic calculations have demonstrated that the formation of heteroligand complexes is always energetically more favourable than the formation of homoligand complexes [15–20]. Heteroligand complexes can be formed in two ways. They can be produced when complex formation with one ligand gives rise to coordination-unsaturated compounds. The second ligand can then be incorporated by occupying some or all the remaining coordination sites at the metal ion. The second possibility occurs when a single-ligand complex is in fact saturated but not all the valences of the inorganic ion have been compensated. Under these conditions, the heteroligand complex is formed by association of the second ligand and the first charged complex. The formation of the association complex of chlorogallate with diantipyrinylmethane or its detivatives ($GaCl_4$–DAPM), which can be extracted with chloroform, as well as numerous association complexes described by Blyum [21] and other workers [22–26] may serve as typical examples.

The chemistry of transition metal complexes in solution is to a large extent concerned with the chemistry of heteroligand complexes. The wide variety of heteroligand complexes (MX_mY_n) can be accounted for by their higher stability in solution compared with complexes containing identical ligand species. The formation of complexes with different ligand species also leads to appreciable changes in the physicochemical properties of the compounds: changes in their optical properties, an increase or decrease of solubility, and the appearance of capacity to be extracted by organic solvents; it is therefore useful to employ the extraction of coloured heteroligand complexes containing an organic complex-forming agent (for example polyphenols) as one of the ligands. However, one of the main advantages of heteroligand complexes is the possibility of a great increase in the sensitivity and selectivity of analytical reactions owing to their high coordination capacity. The absorption spectra of such complexes differ from those of homoligand systems.

Here, one should emphasise that, since analytical chemistry is concerned with solution chemistry, the majority of analytical reactions are based on the use of heteroligand complexes and, according to Pilipenko and Tananaiko [27], the formation of heteroligand complexes in solution is the rule rather than the exception. The contrary view was held previously. Bearing in mind that, apart from the main components, a homoligand complex can include water or organic solvent molecules as well as hydroxide ions, which are formed on hydrolysis, the vast majority of analytical systems will prove to be of the heteroligand type.

The role of heteroligand complexes in analytical chemistry can be hardly overestimated. Hundreds of spectrophotometric and extraction-photometric methods for the determination of inorganic ions are based on the use of heteroligand complexes. During the last 8 years (1966 to 1973), more than 600 papers dealing with such complexes were published. The text below deals with the applications of heteroligand complexes in one of the most difficult branches of analytical chemistry, namely the analysis of niobium and tantalum [28].

II. SPECTROPHOTOMETRIC DETERMINATION OF NIOBIUM AND TANTALUM IN HETEROLIGAND COMPLEXES

1. METAL COMPLEXES WITH TWO DIFFERENT ELECTRONEGATIVE LIGANDS

Until recently, it was believed that reagents such as metallochromic indicators do not undergo colour reactions with niobium and tantalum. The explanation was that hydrolysis results in the formation of various relatively inactive hydrolysed and polynuclear species, incapable of reacting with the metallochromic indicators used in weakly acid solutions. However, experiments showed that, in the presence of powerful complex-forming agents (tartrate, oxalate, and fluoride ions, etc.), certain organic reagents undergo highly differentiating colour reactions with niobium and tantalum owing to the formation of heteroligand complexes. One of the ligands decomposes polymeric niobium or tantalum ions and maintains them in solution, while the other (the metallochromic indicator) serves as the chromophore in the stable ternary complex formed[29]. In the chemistry of niobium and tantalum heteroligand complexes play a special role, which serves as a basis for the most highly differentiating, sensitive, and selective modern spectrophotometric methods for the determination of these elements[28].

(a) Complexes with Polyphenols

Tantalum–pyrogallol complexes can serve as an example of heteroligand complexes with two electronegative ligands. In the absence of other complex formation agents, tantalum forms with pyrogallol a colourless complex in an acid medium (with an absorption band at 340 nm); when oxalate ions are introduced into the solution of the tantalum–pyrogallol complex, the band at 340 nm is weakened and a new band appears at 420 nm. The formation of this heteroligand complex constitutes the basis of familiar photometric methods[30-34].

Babko and Lukachina[35] examined the pyrogallol method for the determination of tantalum and niobium in their joint presence, based on the fact that in an acid medium a coloured ternary tantalum oxalate–pyrogallol complex is formed, while the niobium gives rise to a colourless oxalate complex. Thus the differentiating ligand for niobium and tantalum in an acid medium is not pyrogallol but the third component, in the present instance oxalic acid. With increase of pH, the concentration of $C_2O_4^{2-}$ and pyrogallol (Pg^{2-}) ions increases. However, oxalic acid is a stronger acid and therefore at $pH > pK_2$, i.e. at $pH > 4$, and a constant overall oxalic acid concentration, the concentration of $C_2O_4^{2-}$ does not increase, while that of the Pg^{2-} ions derived from the weaker acid (pyrogallol) continues to rise. As a result, with increase of pH, the $C_2O_4^{2-}$ ions are displaced from the coordination spheres of tantalum and niobium and only the pyrogallol complexes remain: the coloured niobium complex and the colourless tantalum complex. On the other hand, in a more acid medium ($pH < 4$), the equilibrium shifts towards the formation of colourless niobium oxalate complexes with displacement of Pg^{2-} from the coordination sphere. The study optimised conditions for the determination of niobium and tantalum. Niobium is determined in a weakly alkaline medium at pH 7–8 with $[Pg^{2-}_{tot}] = 0.2$ and $[C_2O_4^{2-}]$ 0.1 M. Tantalum is determined in the heteroligand complex $[TaOC_2O_4Pg_2]^{3-}$ at 400 nm and pH 2–3 with $[Pg^{2-}] = 1.3$ to 1.4 M and $[C_2O_4^{2-}] \geq 0.2$ M.

The formation of heteroligand niobium complexes with pyrogallol and ethylenediaminetetraacetic acid (EDTA) has been noted. Pyrogallol complexes have been used to develop extraction-photometric methods for the determination of tantalum in the presence of niobium, which are discussed below. Among other polyphenols, heteroligand complexes are formed by tantalum with catechol in the presence of $C_2O_4^{2-}$. A photometric method for the determination of tantalum has been developed on this basis[36,37]. It has been modified[38] by the introduction of EDTA. The author[38] drew attention to the fact that EDTA, which usually decolorises the majority of metal complexes, actually enhances the colour of the catechol complex of niobium and enters into the composition of the heteroligand complexes. Thus one can claim that coloured heteroligand compounds of the type of MX_mY_n are formed in those cases where the chromophore is not one of the ligands but the central atom. The complex was investigated in detail in later studies[39,40]. Nevertheless, the method remains relatively unselective and insensitive. In the measurements of the optical density of the complex in the region of 385–395 nm the influence of niobium is to a large extent eliminated, but titanium interferes.

A number of methods involving tetraphenylarsonium have been described[41,42]. Methods in which tetraphenylarsonium and thiocyanate ions are both used are of considerable interest. Niobium and tantalum peroxide complexes with various organic dyes[43] as well as niobium thiocyanate complexes with benzoylphenylhydroxylamine (BPHA)[44] and with dihydroxy-3,4-phenyl-4-azobenzene[45] can also be included among heteroligand complexes.

Niobium and tantalum tartrate, oxalate, citrate, and peroxide complexes with many metallochromic indicators form part of the group of complexes with different electronegative ligands. Reagents containing hydroxypyridylazo- and *oo*-dihydroxyazo-groups are the most sensitive and give rise to contrasting and deep colours with niobium. These include 4-(2-pyridylazo)resorcinol (PAR) and its derivatives, analogues of lumogallion–bisazo-derivatives of chromotropic acid, and monoazo-compounds based on the R-salt. Azo-compounds with complexone groups are also promising reagents for niobium. Arylmethanes and other basic dyes are the most sensitive and selective reagents for tantalum.

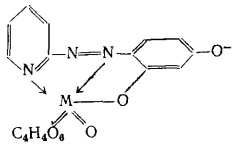
(b) Heteroligand Niobium and Tantalum Complexes of Pyridylazo-compounds

Pyridylazo-compounds are known as reagents forming stable ternary metal–reagent–ligand complexes with niobium and tantalum[46]. Complexing agents used to solubilise these elements, namely peroxide, oxalate, tartrate, and citrate ions, are normally used as the third components.

Among reagents of the pyridine series, 4-(2-pyridylazo)resorcinol has been most thoroughly investigated. It has been proposed as a highly sensitive reagent (molar extinction coefficient of about $3.5\ 10^4$) for the photometric determination of niobium and tantalum in weakly acid solutions (pH 5–6) in tartrate[47-49], peroxide[50], or oxalate[51] solutions. Pyridylazo-compounds are highly reactive but relatively unselective. The explanation is that salt-forming compounds of the type of PAR give rise to complexes with ions having small radii and high positive

charges, i.e. heavy metal and transition metal ions, which thereby complete their *d* and *f* shells[52]. Apart from niobium and tantalum, PAR forms coloured complexes with 40 elements (U, Co, Ga, In, the lanthanides V, Pb, Cu, etc.)[53,54].

In order to choose conditions under which the greatest sensitivity and selectivity of the reactions of niobium and tantalum with PAR are attained, a detailed study was made of the complexes formed by PAR and its analogues with the above elements[55,56]. It has been established that coloured niobium and tantalum complexes are formed by reagents of the pyridyl series (12 such compounds have been investigated) which contain the OH group in the *ortho*-position relative to the diazo-group. In these compounds OH groups or other electron-donating groups, which are in the *para*-position relative to the azo-group, play the role of groups active in analysis, which sharply increase the sensitivity of the reagents. It has been demonstrated[55,56] that niobium and tantalum form heteroligand complexes with pyridylazo-compounds and complex-forming ligands (tartrate, oxalate, fluoride, etc.) with a valence bond via the hydroxy-group in the *ortho*-position relative to the diazo-group and a coordinate bond via the nitrogen of the azo-group:



The high reactivity of PAR in reactions with niobium and tantalum can be explained to some extent by the formation of such compounds. The tartrate ions (or other similar ligands), which enter into the composition of the complex as the third component, disrupt the polymeric niobium and tantalum ions and maintain them in solution in a monomeric form, while the organic reagent—the metallochromic indicator (PAR) and its analogues—plays the role of the chromophore in the ternary complex. The existence of such heteroligand complexes has been demonstrated experimentally. 5-(3,5-Dibromo-2-pyridylazo)-monoethylamino-*p*-cresol (3,5-di-Br-PAAC), which forms a coloured sparingly water-soluble complex with niobium in the presence of tartrate ions, has been synthesised. Analysis of the heteroligand complex isolated in a crystalline form showed that its composition can be described by the formula

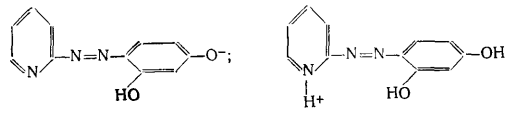
$$\text{Nb - 3,5-di-Br-PAAC - } C_4H_4O_6^2 \cdot 5H_2O,$$

and its molecular weight is 778, i.e. direct confirmation of the formation of a ternary complex with the component ratios Nb : R : tartrate = 1 : 1 : 1 was obtained.

The calculated instability constants of the complexes showed that the most stable complexes are formed by brominated pyridylazo-compounds, which react with niobium or tantalum in more acid media. Consequently, electronegative substituents in the pyridine ring increase the selectivity of the reagents. Two new selective and sensitive reagents were suggested on this basis: 5-(5-bromo-2-pyridylazo)-2-monoethylamino-*p*-cresol (5-Br-PAAC) and 4-(5-bromo-2-pyridylazo)resorcinol (5-Br-PAR), which give rise to a marked bathochromic effect ($\Delta\lambda$ = 130–160 nm) and high molar extinction coefficients (4.17×10^4 and 3.8×10^4 respectively). The determination of niobium and tantalum with the aid of the proposed reagents in highly acid solutions (up to an HCl concentration of 2 M) is not interfered with by molybdenum, tungsten, uranium, zirconium, titanium, iron, rhenium, and other elements.

4-(2-Thiazolylazo)resorcinol (TAR) has a structure similar to that of PAR and like the latter forms with niobium coloured complexes in weakly acid solutions (pH 5–5.5). However, thiazolylazo-compounds, containing the less basic thiazole ring instead of the pyridine ring, should give rise to niobium complexes in more acid media and hence should be more selective than pyridylazo-compounds. 5-(2-Thiazolylazo)-2-monoethylamino-*p*-cresol (TAAC) is of considerable interest in this respect; a method for the determination of niobium in alloys containing uranium, zirconium, and molybdenum involving the use of TAAC has been developed[57].

Studies have shown that, in contrast to other media, in tartrate solutions the heteroligand PAR complex of niobium is formed not only at pH 5–6 but also at higher acidities (HCl concentrations in the range 0.5–1 M),[49] different compounds being formed, since the ionic state of PAR depends greatly on the acidity. At pH 5–6 a proton dissociates initially from the OH group in the *para*-position with formation of a singly charged ion in solution[53,58]. In the solution where [HCl] = 1 *N* PAR exists in the form of a singly charged cation as a result of the protonation of the heterocyclic nitrogen of the pyridine ring:



(pH 5–6) (1 M HCl)

The absorption spectra of these compounds differ from one another[59]. The ternary complex has an absorption maximum in 1 M HCl solution only in the region of 405 nm, while at pH 5–6 the maximum is at 520–540 nm (depending on the nature of the third complex-forming component). Furthermore, in weakly acid media a second indistinct maximum is also observed in the region of about 400 nm, which is extremely characteristic of heteroligand complexes. Since the absorption maximum of the complex in an acid solution is close to that of the reagent (395 nm), a differential curve with a maximum at 540 nm was used in practice. In an acid solution we have the ratio Nb : PAR = 1 : 2 (instead of 1 : 1 at pH 5–6). With increase of acidity, there is a sharp increase of the selectivity of PAR. Iron, aluminium, titanium, zirconium, molybdenum, tungsten, the lanthanides, and other elements do not interfere with the determination of niobium.

Methods have been developed for the determination of niobium under such conditions in steels[60], minerals[59], and complex copper-based alloys[61]. A differential method has been devised for the determination of large amounts of niobium in alloys and ferroalloys[62], particularly in ferroniobium.

Masking of tantalum with a large excess of tartrate ions made it possible to develop a procedure for the determination of niobium and tantalum without their separation[63]. In tartrate solution tantalum is bound in a stable polynuclear complex, with a polymerisation factor of about 670, which does not form compounds with PAR, and therefore in 3–4% ammonium tartrate solutions at pH 4.5–4.8 tantalum does not interfere with the development of the colour of the PAR complex of niobium. The method proved to be extremely effective and permits the determination of 0.1%

of niobium and more in tantalum concentrates and in metallic tantalum. The heteroligand PAR complex of tantalum has been used to determine tantalum in steels and alloys with a high tantalum content [64]. It has been shown that, in the presence of ligands used to solubilise niobium and tantalum (oxalate, citrate, etc.), PAR forms coloured complexes with both tantalum and niobium. The most sensitive and stable complex is formed in 0.01 M citrate solution at pH 5.4. Under these conditions, niobium does not form a coloured compound. However, a concentration corresponding to more than 1 mg of niobium in 50 ml increases the optical density of the tantalum solution. Stable and reproducible results can be obtained only for the same reactive tantalum species, which is achieved by selecting identical conditions for the preparation of solutions of the sample and standard solutions (boiling of the initial solutions at the same pH 2.3–2.8 after dissolving the alloys, introduction of nickel into standard tantalum solutions). When the steel specimen contains less than 5% of tantalum, the latter is determined relative to a standard steel specimen and not with the aid of a calibration graph [64].

Thus, using heteroligand PAR complexes, it is possible to increase greatly the selectivity in the determination of niobium and tantalum. Ways of increasing the selectivity still further, involving the use of reagents with electronegative substituents and the ligands of the heteroligand complex as masking agents (tartrate and citrate) as well as an increase of acidity in the preparation of PAR complexes of niobium, have been discussed [65].

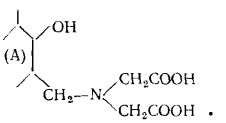
Other complexes of resorcinol derivatives have also been investigated. A method has been determined for the determination of niobium as a heteroligand complex with H_2O_2 and sulphonaphtholazoresorcinol [66]. In another study H_2O_2 was used in combination with morin [67]. The fluorescence method developed with the aid of these reagents makes it possible to determine niobium with a sensitivity of 0.004 $\mu g\ ml^{-1}$.

(c) Heteroligand Niobium Complexes with *oo'*-dihydroxyazo-compounds

Organic compounds containing the *oo'*-dihydroxyazo-group undergo extremely characteristic colour reactions with niobium. Compounds of this type can be divided into two groups on the basis of their structural features. The first includes Lumogallion and many bisazo-derivatives of chromotropic acid—structural analogues of Arsenazo III (Sulphochlorophenol S, Sulphomethanylphenol Nitrosulphophenol S, and others) and the second group includes Anthracene Chrome Violet and other monosubstituted R-salt derivatives (Picramine R, Magneson, Picramine-epsilon, etc.); they all form heteroligand complexes with the niobium tartrate complex or with niobium complexes of other hydroxy-acids. In the first group of reagents Sulphochlorophenol S or 3,6-bis[(5-chloro-2-hydroxy-3-sulphophenyl)azo]-4,5-dihydroxynaphthalene-2,7-disulphonic acid (SCPS) is of greatest interest. This dye is widely used to determine niobium [68–72]. The most interesting compound in the second group is Picramine R or 3-hydroxy-4-[(2-hydroxy-3,5-dinitrophenyl)azo]naphthalene-2,7-disulphonic acid. Both reagents, SCPS and Picramine R, form coloured complexes with niobium at a high acidity of the solution, are satisfactorily selective, and permit the determination of niobium in metals and alloys without the separation of components. SCPS and its analogues are three times more sensitive ($\epsilon = 3.6 \times 10^4$) than Picramine R ($\epsilon = 1.1 \times 10^4$). SCPS is used to determine microamounts of niobium in metals [73], while Picramine R is used for the determination by photometric or differential methods of large amounts of niobium in alloys and intermetallic compounds containing up to 70–80% of niobium [74].

(d) Heteroligand Niobium Complexes with Metallochromic Indicators Containing Complexone Groups

The importance of heteroligand complexes for the determination of niobium and tantalum can be readily demonstrated for reagents containing complexone groups: Xylenol Orange (XO) and Methylthymol Blue (MTB). It appeared likely that these reagents, which do not contain an OH group in the *ortho*-position relative to the azo-group (a characteristic of niobium and tantalum reagents), are capable of forming complexes with these metals. Indeed, in the first relevant reports the reaction of niobium with Xylenol Orange was classified as insensitive, because the experiments were performed without additional ligands (oxalate or tartrate ions) at room temperature. Later it was found that, in the presence of either of these ligands, an intensely coloured complex is formed on heating. A fairly stable niobium complex is known to be formed at pH 3–3.5 with EDTA, while tantalum forms a fairly weak complex with this substance. Similarly, XO and MTB, which contain complexone groups, form in oxalate or tartrate solution at pH 2–4 fairly stable brightly coloured complexes with niobium and interact only weakly with tantalum. XO has been proposed as a reagent for niobium by Babko and Shtokalo [75] and has been used to determine niobium in certain alloys [76]. MTB has been investigated as a reagent for niobium by Elinson and Mirzoyan [74]. The fact that niobium reacts with MTB in 1 : 1 molar proportions, while in the absence of sufficient oxalate or other similar ligands the niobium–MTB complex is not formed at all suggests that, as for pyridylazo-compounds, oxalate ions enter into the composition of the coloured compound, forming a heteroligand complex with the component ratios $Nb : C_2O_4^{2-} : MTB = 1 : 1 : 1$. Oxalate and tartrate ions decompose polymeric niobium ions. At pH 2–3 niobium readily hydrolyses and in the absence of these ligands could not compete with the MTB or XO protons in the formation of a complex. Experiments have shown that the formation of MTB and XO complexes of niobium is due to the group (A), i.e. to the most reactive hydroxy-, amino-, and carboxy-groups:



2. DETERMINATION OF NIOBIUM AND TANTALUM IN THE FORM OF COMPLEX HETEROPOLYACIDS

Niobium and tantalum form heteroligands phosphorus–niobium–molybdenum complexes which are more stable and more soluble than the usual heteropolyacids. The absorption bands of these complexes are displaced further towards the visible region, while the reduced binary tantalum–molybdenum complex absorbs in the infrared ($\lambda = 820$ nm). [78] The phosphorus–niobium–molybdenum complex can be reduced to a blue complex, the intensity of

the colour of which is proportional to the concentration of niobium (sensitivity 0.1 μg ml^{-1}). The conditions governing this reaction have been refined [79] and methods have been developed for the determination of niobium in ores together with a differential spectrophotometric method for the determination of large amounts of niobium [80]. Titanium interferes with the determination of niobium; the influence of tungsten can be eliminated by an excess of phosphate. Methods for determination of niobium and titanium in alloys [81] and of niobium in steels [82] have been developed on the basis of the formation of heteroligand heteropolycomplexes. A technique has been devised for the determination of low niobium concentrations based on the formation of niobium–molybdenum blue [83].

3. COMPLEXES WITH TWO DIFFERENT ELECTROPOSITIVE ATOMS AND ONE ELECTRONEGATIVE LIGAND

Complexes with two electropositive metals have not found such extensive application as heteroligand complexes with two electronegative ligands. However, it is possible to quote certain instances of the formation of mixed niobium and tantalum complexes with an electronegative ion, whereupon tantalum becomes an obstacle, which is difficult to overcome, to the determination of niobium when the two metals are present jointly in large amounts. For example, compounds are formed by mixtures of niobium and tantalum with H_2O_2. Niobium combines with one H_2O_2 molecule so strongly that in a weakly acid medium it is not titrated by potassium permanganate. When an excess of a standardised H_2O_2 solution is added, the concentration of niobium can be determined in the absence of tantalum by titrating the free H_2O_2 with permanganate [84], but in the presence of tantalum niobium does not retain the H_2O_2 molecule in consequence of the formation of a mixed niobium–tantalum peroxide complex. In the presence of phosphoric acid the niobium peroxide complex decomposes, whereupon only tantalum forms a stable peroxide [85].

Another example involves the formation of mixed niobium–tantalum complexes with tartrate ions. In the method developed for the determination of niobium in the presence of large amounts of tantalum with the aid of PAR [63] at pH 4.5–4.8 it is possible to bind tantalum with a large excess of tartrate ions into a stable relatively unreactive polynuclear complex and thus avoid the formation of a mixed niobium–tantalum complex with PAR. Niobium can then be determined with a high accuracy even in metallic tantalum [63]. In the determination of large amounts of niobium (10–80%) by a differential spectrophotometric method with PAR more than 50 μg of tantalum in 1 M HCl solution [62] is already sufficient to interfere with the determination, since in such a solution the tantalum tartrate complex is not sufficiently stable to prevent the formation of a mixed complex with niobium and PAR.

Such interference by tantalum in the determination of niobium has been called by some investigators (Babko, Belcher) "the loss of individual properties", which does not accurately reflect the true behaviour of these elements in solution. We believe it to be a typical instance of the formation of a mixed complex of different metals not with loss but with manifestation of the individuality of elements with similar physicochemical properties (the copolymerisation and complex formation phenomena when the ionic radii are similar, etc.).

Mixed tantalum–zirconium tartrate complexes can serve as an example of mixed complexes of two different metals [86]. Studies by the equilibrium shift and isomal series [continuous variations] methods established that, in 0.5 M tartaric acid solution at pH 2 and in the presence of a tenfold excess of zirconium, a complex with the component ratios Ta : Zr : Tart = 1 : 1 : 2 is formed. The tantalum in the mixed tartrate complex does not react with PAR, [28] which must be taken into account in the analysis of such systems.

III. THE USE OF HETEROLIGAND NIOBIUM AND TANTALUM COMPLEXES IN EXTRACTION PROCESSES

1. EXTRACTION-PHOTOMETRIC METHODS FOR THE DETERMINATION OF NIOBIUM

A number of compounds which constitute the basis of extremely sensitive and selective extraction-photometric methods for the determination of niobium and tantalum belong to the group of heteroligand complexes formed when niobium or tantalum interact with two electronegative ligands.

Extraction is a widely used procedure for improving the sensitivity and selectivity of analytical reactions; in this way it is possible to increase sharply the sensitivity of photometric methods.

Extraction with formation of heteroligand complexes can be described by the equation

$$M^{z+}(w) + mH_aX(w) + hH_bY(o) \rightleftarrows MX_mY_n(o) + (am + bn)H^+(w), \quad (4)$$

where w is the aqueous fraction and o the organic fraction. Numerous extraction-photometric methods are based on the measurement of the optical density of the compound $MX_mY_n(o)$ formed in the organic phase. If the partition coefficient of MX_m is very small, the affinity of HbY for MX_m plays a significant role. The equilibrium in the system shifts continuously during the extraction process towards the formation of MX_mY_n and a higher partition coefficient may be obtained for MX_mY_n than for MX_m.

The extraction of complexes in the presence of hydrophobic organic bases is especially important in analytical chemistry. Studies have shown, for example, that the chelate complex of molybdenum and catechol can be extracted from the aqueous phase by organic solvents in the presence of tetraphenylarsonium (as well as in the presence of pyridine) [87]. In this case the occurrence of extraction has been explained by a synergic effect, but the latter is based on the formation of a heteroligand complex. The use of tetraphenylarsonium as well as tetraphenylphosphonium for the extraction of niobium proved to be a fairly effective procedure. In the presence of tetraphenylarsonium niobium also forms with thiocyanate ions the heteroligand complex $[(C_6H_5)_4As]_2[NbO(NCS)_5]$, which can be extracted by organic solvents. The formation of this complex constitutes the basis of the extraction-photometric method for the determination of niobium [88]. Compounds formed by dioctylaminoethanol (DOAE) and fluoride ions with niobium or tantalum are similarly extracted by chloroform as $(DOAE)_2[NbOF_5]$. [89]

In particular complexes of the type $MX_mY_n^0$ or $[MX_m(RY)_n]^0$, where Y is the organic base, can be formed in the extraction process. Whereas in the former case Y provides an electron-donating atom for the formation of an electron pair, coordinating the metal ion, in the latter case Y enters into the association complex in the form of an 'onium compound. Anionic complexes which become capable of forming hydrates by combining with the SO_3H

group form solvates with ammonium, arsonium, or phosphonium cations and are extracted in the form of associated ionic species. A number of extraction-photometric methods based on the extraction of these two types of heteroligand complexes are described below.

In combination with diphenylguanidine, the chlorosulphophenol described above has been used in the extraction-photometric determination of niobium with the aid of 1-butanol. Iron, molybdenum, and zirconium are bound by thioglycolic acid and the complexone [90].

The extraction of complexes containing sulpho-, carboxy-, or hydroxy-groups is based on the fact that alkyl- and aryl-amines and their salts form with niobium complexes substituted ammonium salts (R_3NR) which are readily extracted. Thus heteroligand complexes which are extracted by chloroform are formed in the niobium–salicylic acid–organic base systems [91].

An extraction-photometric method has been proposed for the determination of niobium in the presence of tantalum, titanium, uranium, zirconium, iron, and tin; it is based on the formation of a 1 : 2 : 2 extractable heteroligand complex with SCN^- ions and pyrrolidinedithiocarbamate [92].

The usual catechol and pyrogallol methods for the determination of niobium have been improved by the extraction of polyphenol complexes of niobium in the presence of quaternary ammonium bases having a long hydrocarbon chain, with a consequent sharp increase of the sensitivity of the determination of niobium [93,94]. The influence of tantalum, which is also extracted by the above reagents, was eliminated by selecting optimal conditions. Best results were achieved in the extraction of niobium by polyethoxy-15-stearylmethylammonium chloride [Ethoquad 18125].

A large group of niobium complexes containing two organic reagents, one of which forms with niobium a soluble inner complex and the other a sparingly soluble complex, has been investigated [95,96]. The following compounds (with 1 : 2 : 2 component ratios) are of interest: niobium–pyrrolidine dithiocarbamate–catechol, niobium–BPHA–catechol, niobium–BPHA–pyrrogallol, niobium–cupferron–catechol, and niobium–catechol–diantipyrinylpropylmethane. The compounds are almost completely extracted by chloroform. The method is also interesting because niobium can be determined in the presence of a 20-fold excess of titanium and tantalum. The molar extinction coefficient is $\epsilon = 1.4 \times 10^4$.

The extraction of a number of metals forming heteroligand complexes with Arsenazo I and diphenylguanidine has been studied [97,98]. Niobium, tantalum, titanium, zirconium, hafnium, and thorium can be extracted from acid solutions by pentyl, isopentyl, and butyl alcohols; iron, aluminium, beryllium, scandium, yttrium, lanthanum, and copper can be extracted from weakly acid and neutral solutions. The extraction of niobium and a number of other elements in the form of heteroligand complexes which they form with *o*-carboxy-, *oo'*-dihydroxy-, and hydroxyazo-compounds (Acid Chrome Dark-blue, Eriochrome Black T, Magneson, Acid Chrome Red, and others) and organic cations has been investigated [99]. The extraction takes place over a wide pH range. It has been suggested that ionic association complexes in which inner complexes behave as anions are extracted.

The heteroligand complexes of a large group of metals, including niobium, with Chromazurol and diphenylguanidine are readily extracted and permit the determination of many elements with a high sensitivity [100,101]. Peroxo-complexes of niobium and tantalum react with oxalate ions to form compounds which can be extracted by trioctylamine [102]. Niobium and tantalum can be separated in this way from iron, titanium, manganese, vanadium, aluminium, and other elements. Trioctylamine and certain *N*-substituted amines have been used in inorganic acid solutions for the separation of niobium and tantalum by extraction using chloroform [103–105].

An extraction-photometric method, based on the formation of a heteroligand niobium complex with catechol (CA) and thenoyltrifluoroacetone (TTFA) in the proportions Nb : CA : TTFA = 1 : 2 : 3, which can be extracted by chloroform, has been developed for the determination of niobium. The complex absorbs at 414 nm ($\epsilon_{414} = 7.7 \times 10^3$) and the sensitivity is 2 μg/ml Nb. [106] It was shown recently that mixed niobium–catechol–phenylbenzoylpyrazolone and niobium–thiocyanate–phenylbenzoylpyrazolone complexes with component ratios of 1 : 2 : 1 are readily extracted by organic solvents [107].

The extraction of heteroligand organic complexes of niobium and tantalum by oxine in chloroform [108] or by isobutyl methyl ketone from citrate and chloride solutions and also by 50% solutions of tributyl phosphate in chloroform or cyclohexane [109] is used in the radiometric analysis of tantalum–niobium preparations.

It was pointed out above that quaternary heteroligand complexes are used in spectrophotometric analysis, particularly when extraction processes are resorted to. A typical example is provided by the extraction of niobium in the form of a heteroligand complex with Catechol Violet (CV), pyridine, and potassium bromide [110]:

$$2Nb(OH)_2^{3+} + PyH^+ + H_3CV^- + 3Br^- \rightarrow \{[Nb(OH)_2]_2CVPyH\}^{3+}Br_3^- + 3H^+.$$

In this compound pyridine is bound to the sulpho-group of Catechol Violet, and Br^- is an outer-sphere anion, which neutralises the positive charge of the complex formed. A quaternary system is produced with the component ratios Nb : CV : Py : Br = 2 : 1 : 1 : 3. The coloured compound is formed immediately after mixing the solutions and remains stable for 32 h. The coloured solutions obey Beer's law in the presence of 15–100 μg of niobium in 25 ml ($\epsilon = 3 \times 10^4$).

2. EXTRACTION-PHOTOMETRIC METHODS FOR THE DETERMINATION OF TANTALUM

The extraction-photometric methods for the determination of tantalum are based on the use of heteroligand ionic association complexes. Such association complexes are formed when tantalum fluoride complexes interact with basic dyes. The coloured heteroligand complexes formed can be extracted by inorganic solvents, such as benzene, toluene, xylene, chloroform, etc. Under certain conditions, the pure dye is hardly extracted by these solvents. The formation reactions of the extractable ionic association complexes are fairly sensitivity and specific. The following dyes are used as the reagents: triarylmethane dyes (Methyl Violet, Brilliant Green, Crystal Violet, Malachite Green, etc.), xanthene dyes (Rhodamine 6G, Rhodamine S, and Rhodamine 3B), oxazine dyes (Nile Blue, Meldola's Blue, New Blue, etc.), and thiazine dyes (Methylene Blue, Methylene Green, etc.). In the association complexes formed tantalum in the form of the negatively charged fluorotantalate ion substitutes the acid residue (Cl^-, HSO_4^-) in the dye. A number of studies have been made on the use of triarylmethane dyes (TAMD) and xanthene dyes for the determination of tantalum in various materials. These procedures have been reviewed in detail in a monograph [28].

Recently much attention has been devoted to the problem of the mechanism of the formation of association complexes of fluorotantalate with triphenylmethane dyes (TPMD). Most investigators tend to regard the complex anion TaF_6^- as the reactive species in the interaction of fluoride solutions of tantalum with TPMD.[111,112] Elemental analysis of the organic phase in the extraction of the fluorotantalate of Brilliant Green with chloroform established that the compound extracted has the formula $RTaF_6$,[113] where R is the cation of the basic dye. This was confirmed in other investigations.

It was suggested previously that the extractability of ionic association complexes depends on the charge, the relative dimensions of the anion and cation, and the presence of hydrophobic groups in one or both ions. The ratio of the charge to the number of atoms in the ion was proposed as a criterion of extractability. The extractability of the association complex should improve with decrease of "the specific charge". Lomonosov and coworkers[114-117] demonstrated the inadequacy of these ideas, which fail to take into account the individual characteristics of the cation and anion structures. They showed that the overall effective positive charge in the region of the dye cation involved in association can serve as a criterion governing the choice of TAMD for extraction. It was suggested that the part of the cation bounded by the two most basic parts of the dye is responsible for association. The substituents in the amino-groups in the *para*-positions relative to the central carbon (or nitrogen) atom play an important role here. The presence of such substituents leads to an increase of the positive charge at the ends of the molecule and to the stabilisation of the ionic association complexes formed by the reagent with these substituents. Two reagents of the group of oxazine dyes proposed recently for the extraction-photometric determination of tantalum can serve as typical examples, namely Capri Blue[118] and Meldola's Blue[119]. With Capri Blue, which contains a much greater number of substituents than Meldola's Blue, a more stable structure is produced: the fluorotantalate interacts simultaneously with two substituted groups and this is accompanied by a greater localisation of the positive charge than in Meldola's Blue.

The basicity of the dye, which in the case of TAMD is determined by the electron density at the central carbon atom, can serve as a criterion of the extractability of ionic association complexes. The extractability of TPMD increases steadily in the series Crystal Violet < Malachite Green < Brilliant Green, i.e. with increase of the overall positive charge on two dialkylamino-groups. In extraction at high pH values the conversion of the ionic form of the dye into a carbinol is very important, while at high acidities (2 M H_2SO_4) the influence of protonation becomes more marked. In the case of Brilliant Green, which has more positive electron-donating groups than Malachite Green, this factor has a decisive influence on the extraction. Brilliant Green proved to be the most sensitive dye in the TPMD group and has recently been used widely not only for the extraction-photometric determination of tantalum[28,120,121] but also for the extraction-gravimetric determination of large amounts of this metal[122].

The assortment of reagents used in the form of ionic association complexes with fluorotantalate has been greatly extended during the last 5–6 years as a result of the employment of thiazine dye cations, namely those of Methylene Blue and Methylene Green[123], dimethylthionine, trimethylthionine, and Toluidine Blue[124,125].

The use of oxazine dyes (Capri Blue, Meldola's Blue) has already been discussed[118,119]. Studies are being continued on the Rhodamines (Rhodamine 6G) and the TPMD group is being expanded as a result of additions to the TAMD group—Victoria Blue 4R and B[126] and others. The association complex formed by fluorotantalate and tetra-n-pentylammonium bromide $[(C_5H_{11})_4N][TaF_6]$, is used for the gravimetric determination of tantalum[127].

IV. HETEROLIGAND COMPLEXES IN TITRIMETRIC AND GRAVIMETRIC METHODS FOR THE DETERMINATION OF NIOBIUM AND TANTALUM

Classical gravimetric and titrimetric methods involving complex processes for the separation of niobium and tantalum and their separation from other elements do not meet modern requirements for production control and only spectrophotometric methods employing organic reagents are widely used nowadays. Nevertheless, as a result of the application of heteroligand complexes, gravimetric and volumetric methods for the determination of niobium and tantalum are again resorted to, albeit not very frequently. The methods where the precipitants are quaternary ammonium and tetraphenylarsonium salts, which permit the development of highly selective and sensitive gravimetric procedures, are of special interest. Thus a method has been devised for the precipitation of niobium or tantalum from fluoride solutions (1–8 M) with the aid of tetraphenylarsonium chloride, which permits a quantitative separation of these elements from those in adjacent Groups: tungsten, molybdenum, titanium, and zirconium[128].

Niobium can be separated from tantalum in the form of the complex $[Fe(o\text{-phen})_3][NbO_2(C_4H_4O_5)_2]$ with the aid of ferroin in a solution containing tartrate ions; a gravimetric method for the determination of niobium has been developed on this basis[129]. In the presence of H_2O_2 niobium forms with complexones (ethylenediaminetetraacetate and nitrilotriacetate) ternary complexes with the component ratios Nb : H_2O_2 : complexone = 1 : 1 : 1. Optimal conditions for the existence of these complexes obtain at pH 2–7. In the titrimetric determination niobium peroxide is titrated with nitrilotriacetic acid using Xylenol Orange as an indicator[130]. Owing to the low stability of niobium complexonates, complexometric methods cannot be regarded as sufficiently accurate.

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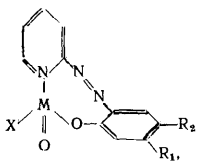
In the theory and practice of the application of heteroligand complexes there are still many obscure and unsolved problems, which are particularly complicated in the analytical chemistry of niobium and tantalum, bearing in mind the complexity of their ions and compounds and their unusual behaviour when present jointly in solutions and in the presence of other metals and organic ligands. Koch and Ackermann[131] showed in a number of instances that the addition of an auxiliary complex-forming agent leads to an appreciable improvement of the reproducibility of the photometric reactions. In particular, referring to a study of niobium–tartrate–PAAC ternary complexes by Elinson and Mal'tseva[55], they suggest that the formation of the heteroligand complex plays an important role in the suppression of the hydrolysis of niobium. The auxiliary ligand can also influence the kinetics of the complex formation reactions and can promote the formation of coloured ions by reaction with the metallochromic indicator.

It has been shown[56] that the niobium complexes formed with pyridylazo-compounds and tartrate or oxalate ions have the following structure:



where $X=C_4H_4O_6^{2-}$ or $C_2O_4^{2-}$;

$R_1=-OH, -N\langle^{H}_{C_2H_5}$ or $-N\langle^{C_2H_5}_{C_2H_5}$;

and $R_2=-H, \quad -CH_3$.

This structure of the complex, involving the formation of the two most probable stable five-membered rings, is justified from the standpoint of the energy state of the system. It has been stated in the literature that in the synthesis of heteroligand complexes five- and six-membered complexes are formed in most cases. Accurate measurements of the dependence of the stability of the complexes on the number of rings formed have not so far been made in relation to binary systems. The number of experimental data is still less adequate for the solution of this problem in relation to heteroligand complexes.

The affinity of the metal ions for specific electron-donating atoms of the complexing agents (usually for O, N, and S) found for binary chelates applies also to heteroligand complexes, but in this case account must be taken of the more complicated interaction with the third component.

Studies have shown[28] that compounds containing hydroxypyridylazo-, *oo'*-dihydroxyazo-, and complexone groups are the most sensitive and selective reagents for niobium. These groups, which are involved in colour reactions with the niobium present in heteroligand complexes, contain two OH groups in the *ortho*-position relative to the azo-group (*oo'*-dihydroxyazo-compounds) or one OH group with the heterocyclic nitrogen atom playing the same role as the second OH group (pyridylazo-compounds), while in compounds containing complexone groups, which play the role of azo-groups, there are two OH groups in the *ortho*-positions in relation to them.

Sensitive colour reactions with niobium are undergone only by those reagents which contain, apart from ring-forming groups, also auxochromes; many electron-donating and electron-accepting substituents, frequently in the *para*-position relative to the azo-group, behave as auxochromes.

The most sensitive and selective reagents for tantalum are those capable of forming heteroligand complexes in the form of associated ionic species with fluorotantalate. These include basic triarylmethane dyes and their analogues.

Studies on heteroligand niobium and tantalum complexes with the above groups of reagents led to the development of precision methods for the determination of niobium and tantalum in various materials in the presence of many elements without their separation.

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Reactivity and Transmission of Electronic Effects in Bridged Bicyclic Systems

L.M.Litvinenko, R.S.Popova, and A.F.Popov

Analysis of data for the transmission of electronic effects in various biaryl systems has shown that the introduction of a bridge group between two benzene rings can both weaken and enhance the interaction between a substituent and a functional centre located in different rings. The nature and mechanisms of the enhanced transmission of electronic influences in bridged systems, called the positive bridge effect (PBE), have been examined and the principal conditions for the manifestation of PBE have been formulated.
The bibliography includes 192 references.

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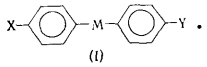
I. INTRODUCTION

Extensive experimental data have now accumulated whose interpretation led to the discovery of certain general relations between the structure and properties of organic substances, which are very important for a quantitative theory of organic reactions [1-9]. The corresponding relations for benzene derivatives have been established from a large amount of data [1-6], but more complex systems have so far been inadequately studied. Investigation of aromatic compounds, which can be represented by structures of type (I), is of undoubted interest for the elucidation of quantitative relations governing the transmission of electronic effects in extended molecular systems:



(I)

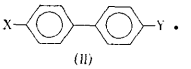
Here X is a substituent which influences the functional group Y and M is a bridge which consists either of a carbon-containing group ($-CH_2-$, $-CH_2-CH_2-$, $-CH=CH-$, $-C\equiv C-$, etc) or a heteroatomic unit (-O-, -S-, -Se-, -NH-, -N=N-, etc).

These compounds are now the subject of very comprehensive studies directed to the elucidation of both their detailed properties and the transmission of electronic effects in their molecules. Various chemical (determination of thermodynamic constants, kinetic measurements, and polarography) and physical (electron diffraction, ultraviolet, infrared, and Raman spectroscopy, NMR, and ESR) methods have been used for the solution of these problems. It is noteworthy that the experimental results themselves and their interpretation in various studies are sometimes contradictory. We therefore believe that it is extremely desirable to compare and discuss together the entire data concerned with the present problem.

It is important to note that compounds of type (I) are now used in a wide variety of fields of practical organic chemistry: in the manufacture of semiconductor materials [10], dyes [11], and physiologically active substances in pharmaceutical preparations [12-14], for the preparation of polymeric materials and their stabilisers [15,16], in the synthesis of reagents for analytical chemistry [17], etc.

II. THE BIPHENYL SYSTEM

The non-bridged biphenyl system (II) is interesting because it can serve as a standard for the comparison of transmission efficiencies in the series of bridged bicyclic systems (I).



(II)

When the problem of the reactivity of biphenyl derivatives was considered, it was initially assumed that the benzene rings act independently in the chemical sense: substituents in one ring do not influence the chemical reactivity of the other ring [18,19]. This conclusion was reached almost exclusively on the basis of the directing influence of substituents in biphenyl and its derivatives in electrophilic substitution reactions. However, this postulate was disproved by the results of Berliner and Blommers [20], who showed in a study of the dissociation of various derivatives of biphenyl-4-carboxylic acid that there is a relation, described by Hammett's equation, between the dissociation constant of the carboxy-group in one benzene ring and the electronic nature of the substituent in the other.

Systematic studies on the transmission efficiencies of biphenyl and other extended molecular systems have been made [21-32], the transmission efficiency being estimated from data for the reactions of the corresponding amines [Y = NH_2 in (I) and (II)] with *p*-nitrobenzoyl chloride (PNBC) and picryl chloride (PC) in benzene. These reactions are interesting because they are extremely sensitive to structural changes in the molecule of the amino-derivative (the ρ^0 for substituted anilines in the above reactions are respectively -3.10 [21,22] and -4.98 [21,23,34]).

Table 1. Transmission coefficients in benzene and biphenyl systems.

No.	Reaction series[a]	X-C$_6$H$_4$-Y standard ρ_{st}	System (II) ρ	System (II) π'
1	ArCOOH ⇄ ArCOO$^-$ + H$^+$; 20°, 50% butylcellosolve-water[20,35]	1.32	0.49	0.37
2	ArCOOH ⇄ ArCOO$^-$ + H$^+$; 25°, H$_2$O[36]	1.00	0.32	0.32
3	ArCOOH ⇄ ArCOO$^-$ + H$^+$; 25°, 50% EtOH — H$_2$O[36]	1.69	0.48	0.28
4	ArCOOEt + OH$^-$ → ArCOO$^-$ + EtOH; 25°, 88% EtOH — H$_2$O[37]	2.57	0.62	0.24
5	ArCOOH + Ph$_2$CN$_2$ → ArCOOCHPh$_2$ + N$_2$; 30°, EtOH[38]	0.95	0.22	0.24
6	ArNH$_2$ + 2,4,6-(NO$_2$)$_3$C$_6$H$_2$Cl → 2,4,6-(NO$_2$)$_3$C$_6$H$_2$NHAr + HCl; 25°, C$_6$H$_6$[31,33,34]	−4.98	−1.56	0.31
7	ArC$_6$H$_4$NH$_2$ + 2,4,6-(NO$_2$)$_3$C$_6$H$_2$Cl → 2,4,6-(NO$_2$)$_3$C$_6$H$_2$NHC$_6$H$_4$Ar + HCl; 25°, C$_6$H$_6$[31,34]	−1.56	−0.49	0.31[b]
8	ArNH$_2$ + C$_6$H$_5$COCl → C$_6$H$_5$CONHAr + HCl; 25°, C$_6$H$_6$[34,39,40]	−3.23	−1.07	0.33
9	ArNH$_2$ + 4-NO$_2$C$_6$H$_4$COCl → 4-NO$_2$C$_6$H$_4$CONHAr + HCl; 25°, C$_6$H$_6$[22]	−3.10	−1.40	0.45
10	ArNH$_2$ + 4-NO$_2$C$_6$H$_4$SO$_2$Br → 4-NO$_2$C$_6$H$_4$SO$_2$NHAr + HBr; 25°, C$_6$H$_5$NO$_2$[41,42]	−3.82	−1.44	0.38
11	ArNH$_3^+$ ⇄ ArNH$_2$ + H$^+$; 25°, H$_2$O[43,44]	2.60	0.89	0.34
12	ArNH$_3^+$ ⇄ ArNH$_2$ + H$^+$; 20°, 50% EtOH — H$_2$O[35]	−3.00	−0.72	0.24
13	ArOH ⇄ ArO$^-$ + H$^+$; 20°, H$_2$O[45]	2.11	0.62[c]	0.29
14	ArSi(CH$_3$)$_3$ + H$_2$O → ArH + (CH$_3$)$_3$SiOH; 50°, CH$_3$COOH — H$_2$SO$_4$[46]	−4.35	−1.33	0.30
15	ArCOCH$_3$ + C$_2$H$_5$OD ⇄ ArCOCH$_2$D + C$_2$H$_5$OH; 20°, EtOH[47]	1.60	0.40	0.25
16	ArOH ⇄ ArO$^-$ + H$^+$; 20°, 60% dioxan-water[48,49]	2.81	0.76	0.27
17	ArOH ⇄ ArO$^-$ + H$^+$; 20°, 60% EtOH — H$_2$O[49]	2.88	0.81	0.28
18	ArOH ⇆ ArO$^-$ + H$^+$; 20°, 60% acetone-water[50]	2.67	0.99	0.37
		π'_{av}	0.31±0.01	

[a]Here and henceforth the reactions of compounds Ar − Y are considered, Ar being groups corresponding to various derivatives of the standard and given systems (in the present instance X−C$_6$H$_4$ and X−C$_6$H$_4$−C$_6$H$_4$). [b]The coefficient π' was calculated for the *p*-terphenyl system relative to the biphenyl system. [c]Determined from two points for X = H and NO$_2$.

The constants ρ for various reactions involving biphenyl derivatives are presented in Table 1, which includes for comparison the analogous quantities for similar reactions of benzene derivatives. Comparison of the results makes it possible to estimate the transmission efficiency of the system as its length is increased by one benzene ring. The coefficient of transmission of electronic effects $\pi' = \rho/\rho_{st}$ (or ρ^0/ρ^0_{st}), where $\rho(\rho^0)$ is the transmission efficiency in the given system and $\rho_{st}(\rho^0_{st})$ the transmission efficiency in the standard system, is used to characterise quantitatively the above change. It was found that regardless of the nature of the reaction series and its sensitivity to the influence of the substituents (the values of ρ for benzene derivatives vary in the range from +2.88 to −4.98), the second benzene ring invariably decreases the effectiveness of the substituent approximately by a factor of three ($\pi'_{av} = 0.31 \pm 0.01$). A similar change in the transmission of electronic effects has been observed also following the introduction of a third benzene ring (on passing from biphenyl to terphenyl; Table 1, No. 7).

The steric structure of the system can influence significantly its transmission efficiency. A convincing illustration of this is provided by the study of the reactivity of compound (II) with Y = NH$_2$, containing in addition two pairs of permanent substituents in the 3,3′- and 2,2′-positions (reactions with PNBC in benzene at 50°C)[22,23,25-30]. 3,3′-Substituents are known to have little influence on the steric disposition of the benzene rings in biphenyl[52-54] and $\rho = -1.30$ is therefore found to be almost equal to that for system (II) ($\rho = -1.34$). On the other hand, the introduction of 2,2′-substituents of different types increases the dihedral angle φ (the angle between the planes of the benzene rings) from 35–40°[55-59] to about 90°[52-54], which decreases the transmission of effects in the biphenyl system containing 2,2′-substituents such as Cl, Br, CH$_3$, CH$_3$OCO, and i-C$_3$H$_7$OCO approximately by a factor of 1.5 ($\rho \simeq 0.92$). A similar result was obtained also for the introduction of a single bulky substituent in the 2-position, as shown by the basicities of 4-aminobiphenyl ($\rho^0 = -0.52$) and 4′-amino-*o*-terphenyl ($\rho^0 = -0.35$†)[60] derivatives in 50% aqueous ethanol at 20°C.

A study of the same reaction of similar aminofluorene derivatives [Y = NH$_2$ in (II); the 2,2′-positions are linked by methylene units], where the system is coplanar, showed that the transmission efficiency ($\rho = -1.65$) is in this case only 20% higher than in compounds of this type (II)[22,29]. This suggests that the increased planarity of the system entails hardly any increase in its transmission efficiency, since on taking into account the second pathway for the transmission of effects (via the methylene unit) one would expect an increase of ρ approximately by 50% (see the transmission efficiency of diphenylmethane‡ in Table 2). The insignificant influence of the coplanarity of the benzene rings in the fluorene system on the transmission of electronic effects is indicated also by other data[45,46,61].

Apart from the above investigations, undertaken to estimate the transmission of electronic effects via the molecular system of (II) from reactivity data (Table 1), there have also been studies where attempts were made to solve the above problem with the aid of, for example,

†We calculated ρ^0 from the literature values[60] using $\sigma^0_{p\text{-}NO_2} = 0.73$.

‡It is assumed to a first approximation that the transmission efficiencies of the 3,3′- and 4,4′-diphenylmethane systems are approximately the same.

measurements of dipole moments, polarographic reduction (oxidation) half-wave potentials, and ESR, NMR, ultraviolet, and infrared spectra of the corresponding compounds.

Comparison of the dipole moments of 4- and 4,4′-substituted biphenyls revealed[62-64] that there is an appreciable interaction between substituents of different electronic types, which is somewhat reduced compared with the corresponding interaction in benzene. However, it is fairly difficult to estimate quantitatively this weakening from the results of the above studies owing to the difficulty of allowing for different kinds of structural factors (configuration of the system, distance between the substituents), which influence the measured dipole moments. This is even more difficult in systems (I) which will be considered below. Therefore in the present review we shall not deal with these investigations in detail.

The study of the polarographic reduction of various 3′- and 4′-derivatives of 4-nitrobiphenyl to the corresponding radical-anions[65,66] and of their ESR spectra showed that the influence of substituents on their first half-wave potential ($E_{1/2}$) and on their spin densities is satisfactorily consistent with the Hammett equation. Comparison with the analogous results for nitrobenzene derivatives indicates a decreased transmission of electronic effects in the bicyclic system compared with the monocyclic system. A similar conclusion was reached also in a study of the polarographic reduction of a number of 4′-derivatives of 4-acetylbiphenyl.[67] However, we believe that data of this kind should be treated with caution, since it is not altogether clear to what extent the quantity ρ can characterise in this case the transmission efficiency of the system. The point is that in polarographic reduction the electron enters the first vacant orbital of the entire molecule and is only then localised in a particular fragment of the latter. For this reason, the system as a whole must be considered as the reaction centre[68,71]. Therefore the experimental results for the polarographic reduction (oxidation) as well as the ESR spectra of substituted biphenyls probably do not characterise unambiguously§ their ability to transmit electronic effects.

To the same extent the above considerations apply also to the electronic spectra of the compounds. Although numerous studies have been made of the spectra of biphenyl and its various derivatives[72-76], one may conclude on their basis only whether or not there is conjugation between the fragments of the system but nothing can be inferred about the nature of the transmission of electronic effects through the system.

On the other hand, the study of both infrared and NMR spectra, where the "reaction centre" is clearly revealed, makes it possible, in principle, to derive definite information about the transmission of electronic effects in such systems. Indeed it has been established from the N–H stretching vibration frequencies in (II) (Y = NH_2)[43] that the biphenyl system transmits such influences much less effectively than the benzene system. The coefficients π', calculated from the shift of the absorption band maxima corresponding to the symmetric (ν_S) and asymmetric (ν_{as}) stretching vibrations, are 0.31 and 0.37 respectively, i.e. close to the values listed in Table 1. Unfortunately the accuracy of the above investigation is not always very high as yet, so that the experimental errors are sometimes comparable to the measured quantities. For example, in a study of the stretching vibration frequencies of the NO_2 group it was found that the difference $\Delta\nu$ between the wavenumbers of 4-nitrobiphenyl and its 4,4′-dinitro-analogue is only 1 cm^{-1}, which is actually less than the error in the determination of the wavenumbers (usually to within 2 cm^{-1}).[77] Because of this, the choice of a functional group sufficiently sensitive to the substitution is an important problem in such studies[43], since the reliability of the results depends significantly on it. Hence it follows that not all the investigations of infrared spectra are of equal value for a quantitative determination of the transmission efficiencies of the systems considered.

Comparison of the NMR spectra of a series of different benzene and biphenyl derivatives shows quite clearly the attenuating effect of the second benzene ring. This, according to ^1H NMR, this influence for the OH group in phenol derivatives (ρ = 1.54)[78,79] and 4-hydroxybiphenyl derivatives (ρ = 0.712)[80] is reflected by the value π' = 0.46. On the other hand, it is difficult to determine unambiguously the coefficient of transmission of electronic effects through the second benzene ring from the ^{19}F chemical shifts δ for the corresponding derivatives. The point is that the influence of the 4′-substituent is in this case described by the two-parameter equation[81-84]

$$\Delta\delta = \rho_I\sigma_I + \rho_R\sigma_R. \qquad (1)$$

The relation between the constants ρ_I and ρ_R, characterising the sensitivity of a series of compounds to the inductive and conjugation effects of substituents, changes on passing from one series to another. Therefore it is necessary to calculate separately the values of π' for the inductive and resonance effects on the basis of data of this kind[85-87]. It was found that the inductive transmission of effects through the second benzene ring in system (II) (π'_I) changes from 0.50 (in cyclohexane) to 0.33 (in dimethyl sulphoxide). The transmission coefficient of this ring π'_R, estimated from the ρ_R, is almost independent of the solvent and amounts to 0.15.

Thus NMR data (and in many cases infrared spectroscopic data) for benzene and biphenyl derivatives show that, on passing from the former systems to the latter, there is an appreciable weakening of the interaction between the substituent and the functional centre. This weakening is approximately equal to that found from the results of other studies (Table 1). However, there is one factor which somewhat restricts the application of spectroscopic data in a quantitative estimation of the transmission efficiency of extended molecular systems. The sensitivity of the reaction series to the influence of substituents is usually determined by comparing the measured quantities with σ constants. The latter characterise in essence[1-8] the differences between the effects of the substituent on the initial and final (or transition) states of the reaction centre. Therefore, despite the large number of successful applications (Zhdanov and Minkin[6], Chapter VII), the problem of a direct comparison of σ constants with spectroscopic data characterising only one (initial, final, or excited) state of the functional centre still remains open[84,88].

Bearing in mind all the foregoing considerations, we shall concentrate attention primarily on the results obtained in the study of equilibria or reaction rates and those of other investigations will be quoted only whenever convenient.

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§The complexity of the situation can be illustrated, for example, by the following fact. Two straight lines with different slopes and separated by an appreciable distance have been obtained[65,66] on the $E_{1/2}$–σ correlation graph for 4′-substituted derivatives of 4-nitrobiphenyl.

Table 2. Transmission coefficients in systems (I) with saturated hydrocarbon bridges.

No.	Reaction series	System (II)	M = $-CH_2-$ in (I)		M = $-CH_2-CH_2-$ in (I)	
		ρ^0_{st}	ρ^0	π'	ρ^0	π'
1	$ArNH_2 + 2,4,6\text{-}(NO_2)_3C_6H_2Cl \rightarrow 2,4,6\text{-}(NO_2)_3C_6H_2NHAr + HCl$; 25°, C_6 [21,89]	−1.56	−0.95	0.61	−0.71[a]	0.46
2	$ArNH_2 + 4\text{-}NO_2C_6H_4COCl \rightarrow 4\text{-}NO_2C_6H_4CONHAr + HCl$; 25°, C_6 [21,22,89]	−1.40	−0.87[a]	0.62	—	—
3	$ArNH_2 + 4\text{-}NO_2C_6H_4SO_2Br \rightarrow 4\text{-}NO_2C_6H_4SO_2NHAr + HBr$; 25°, $C_6H_5NO_2$ [41]	−1.44	−0.39	0.27	—	—
4	$ArNH_2 + C_6H_5COCl \rightarrow C_6H_5CONHAr + HCl$; 25°, C_6 [22,90—92]	−1.07	−0.48[b]	0.45	—	—
5	$ArNH_3 \leftrightarrows ArNH_2 + H^+$; 25°, H_2O [43]	−0.89	−0.65	0.73	—	—
6	$HON_2ArN_2OH \leftrightarrows HON_2ArN_2O^- + H^+ \leftrightarrows 2H^+ + {}^-ON_2ArN_2O^-$; 18°, H_2O [93]	−1.70[c]	−0.80[c]	0.47	−0.60[c]	0.35
		π'_{av}	0.53±0.06		0.40±0.06	

[a, b] Determined from two points for X = H and NO_2 (a) or H and NH_2 (b). [c] The difference $pK_1 - pK_2$, proportional to ρ, is quoted, since ρ cannot be calculated owing to the lack of the values of σ for the 4'-N_2OH^- and 4'-N_2O groups.

III. SYSTEMS WITH CARBON-CONTAINING BRIDGE GROUPS

The entire data referring to the transmission efficiency of bicyclic systems with carbon-containing bridges can be usefully divided into two conventional groups. One of these includes systems with bridges consisting of saturated hydrocarbon units and the other systems with bridges incorporating multiple bonds.

1. Saturated Groups

The results of studies of the transmission of electronic effects in diphenylmethane and bibenzyl systems, where the benzene rings are separated by $-CH_2-$ and $-CH_2-CH_2-$ groups, are presented in Table 2, which includes also the coefficients π' calculated for them relative to system (II), which clearly indicate the insulating role of the hydrocarbon units. The transmission coefficient of the methylene unit in diphenylmethane (0.53 or 0.58 if the extremely low value of π' for series No. 3 is excluded) proved to be somewhat higher than in aliphatic systems (0.350, [94] 0.360, [3] and 0.388 [7]). This may be due to some involvement of the σ, π conjugation of the C–H bonds of the methylene unit with the benzene rings [32,95]. However, one should bear in mind that, when the capacity of the methylene unit for the inductive transmission of electronic effects ($Z^*_{CH_2}$) is estimated from data for aliphatic compounds where the amino-group is the reactive centre (as in the majority of the series in Table 2), the coefficient increases to 0.470–0.554 [94,96,97] and becomes almost equal to π'_{av} in Table 2. The observed transmission efficiency of a single methylene unit in bibenzyl hardly differs from that in the diphenylmethane system.

The compounds considered were also investigated by other methods. The available ultraviolet spectroscopic [98–100], ESR, and polarographic [101,102] data indicate the insulating effect of the methylene units in these systems. However, for the reasons stated, such data can only yield a qualitatitive idea about the properties of these compounds in which we are interested. As regards the estimation of the transmission of electronic effects in these compounds from infrared spectra, there is a full analogy¶, as for benzene and biphenyl derivatives, with the results obtained in studies on the reactivity of the compounds [43].

The values of π' for M = $-CH_2-$ in Table 2 agree with those determined from NMR data for a series of diphenylmethane derivatives (Y = ^{19}F) [86,87,103]. Thus the coefficients π' for M = $-CH_2-$, $-CHPh-$, $-CH(OH)-$, $-CCH_3(OH)-$, $-CPh(OH)-$, and $-CCF_3(OH)-$, calculated from the ρ_I, are in the range from 0.41 to 0.55 and those calculated from the ρ_R are between 0.34 and 0.50. But, when the transmission coefficient is estimated by a direct comparison of the chemical shifts in the spectra of compounds (I) and (II), then it is found to be in the range from 0.30 to 0.62 for systems of this kind. On the other hand, $\pi' = 0.18$, determined from NMR spectra (Y = ^{19}F) [87] for the two-unit bridge group $-CH_2-CH_2-$, proved to be much lower than the value in Table 2.

2. Groups Containing Multiple Bonds

The transmission coefficients π' for bicyclic systems with unsaturated bridge units such as $-C\equiv C-$, $-CH=CH-$, $-CH=\overset{+}{N}-$, $-N=CH-$, $-N=N-$, $-C_6H_4-$, $-CH=\overset{+}{N}(CH_3)-$, and $-\overset{+}{N}(CH_3)=CH-$ (the reaction centre is to the right of the bridge and the substituent is to the left) are compiled† in Table 3.

Comparison of these data leads to the conclusion that any uncharged two-unit bridge with a multiple bond reduces the ability of the system to transmit electronic effects approximately by a factor of 1.7. Bridges containing only carbon atoms behave in almost exactly the same way as those consisting of one or even two heteroatoms (cf. the coefficients π' for the $-CH=CH-$, $-CH=N-$, $-N=CH-$, and $-N=N-$ bridges).

It is interesting that, on passing from bibenzyl, where there is a two-unit $-CH_2-CH_2-$ bridge (Table 2), to the stilbene and tolane systems, where M = $-CH=CH-$ and $-C\equiv C-$ respectively (Table 3), the influence of the substituents increases only by a factor of 1.5, although the last two compounds represent a classical instance of π, π conjugation of multiple bonds, which is interrupted in bibenzyl by the saturated bridge group.

As regards the ability to transmit electronic effects, the stilbene and tolane systems (Table 3) hardly differ

¶Data [77] where the nitro-group is used as the functional centre constitute the only exception. Here it is almost impossible to reach any conclusions owing to the low sensitivity of this centre to the effect of the substituent [43].

†The azobenzene system, which has no carbon atoms in the bridge, is considered here in view of its structural similarity to stilbene.

Table 3. Transmission coefficients in systems (I) with bridges M containing multiple bonds.

No.	Reaction series	System (II)	M=—C≡C—		M=—CH=CH—		M=—CH=N—		M=—N=CH—		M=—N=N—		M=—C_6H_4—		M=—CH=$\overset{+}{N}(CH_3)$—		M=—$\overset{+}{N}(CH_3)$=CH—	
		ρ_{st}	ρ^0	π'	ρ^0	π'	ρ	π'	ρ	π'	ρ	π'	ρ^0	π'	ρ	π'	ρ	π'
1	$ArNH_2$ + 2,4,6-$(NO_2)_3C_6H_2Cl$ → → 2,4,6-$(NO_2)_3C_6H_2NHAr$ + HCl; 25°, C_6H_6[31,104–106]	—1.55	—0.91[a]	0.59	—0.97[a]	0.62	—	—	—	—	—1.20[a]	0.77	—0.49[a]	0.31	—	—	—	—
2	$ArNH_2$ + 4-$NO_2C_6H_4COCl$ → HCl + + 4-$NO_2C_6H_4CONHAr$; 25°, C_6H_6[22,104–106]	—1.40	—0.83	0.59	—0.94[a]	0.67	—	—	--	—	—0.98[a]	0.70	—	—	—	—	—	—
3	$Ar\overset{+}{N}H_3 \rightleftarrows ArNH_2 + H^+$; 25°, H_2O[43]	0.89	—	—	0.52[a]	0.58	—	—	—	—	—	—	—	—	—	—	—	—
4	$Ar\overset{+}{N}H_3 \rightleftarrows ArNH_2 + H^+$; 20°, 50% EtOH—$H_2O$[107–109]	0.72	—	—	0.42	0.59	—	—	—	—	0.36	0.50	—	—	—	—	—	—
5	$Ar\overset{+}{N}H(CH_3)_2 \rightleftarrows ArN(CH_3)_2 + H^+$; 20°, 50% EtOH—$H_2O$ [2] (Zhdanov and Minkin[6], p.59)	1.20[b]	—	—	0.52[c]	0.43	—	—	—	—	0.53	0.44	—	—	—	—	—	—
6	$ArOH \rightleftarrows ArO^- + H^+$; 25°, 98% MeOH—$H_2O$[110,111]	0.60[b]	—	—	—	—	0.30	0.49	0.37	0.61	—	—	—	—	1.17	1.94	1.95	3.23
7	$HON_2ArN_2OH \rightleftarrows HON_2ArN_2O^- + H^+ \rightleftarrows \rightleftarrows 2H^+ + {}^-ON_2ArN_2O^-$; 18°, H_2O[93]	—1.70[d]	—	—	—1.10[d]	0.64	—	—	—	—	—	—	—	—	—	—	—	—
8	$ArCOOH \rightleftarrows ArCOO^- + H^+$; 25°, 98% MeOH—$H_2O$[111]	0.45[b]	—	—	—	—	—	—	0.28	0.62								
		π'_{av}	0.59		0.59±0.03		0.49		0.62		0.59±0.06		0.31		1.94		3.23	

[a]Determined from two points for X = H and NO_2. [b]ρ_{st} estimated from the values of ρ for benzene derivatives and the coefficient π'_{av} in Table 1. [c]Since the —CH=C(CN)— group is the bridge, this result was disregarded in the calculation of π'_{av}. [d]The difference $pK_1 - pK_2$ is quoted (see footnote c to Table 2).

quantitatively from the diphenylmethane system (Table 2). On this basis, one may conclude that the familiar rule of vinylogy, according to which the electronic influence of the substituent in conjugated systems is transmitted to the reaction centre without appreciable decay (Reutov[112], p. 85) is not confirmed in quantitative studies on this problem (at least in a series of molecular systems resembling those described). This is apparently caused by the decisive role of the inductive mechanism in the transmission of electronic effects in systems of this kind.

When the structure of tolane is compared with those of stilbene and biphenyl, then, in contrast to stilbene which has a *trans*-configuration and a non-coplanar structure[113–116] and in contrast to biphenyl where the hydrogen atoms in the 2,2′-positions hinder the rotation of the benzene ring about the single bond joining them[56–58,117], the tolane system offers the smallest steric hindrance to the electronic interaction between the benzene rings on either side of the acetylene bridge, owing to its linearity and the appreciable distance between the 2,2′-hydrogen atoms[118]. However, this interaction is less pronounced in tolane than in the biphenyl system and is the same as in stilbene. This is most probably due to the fact that the carbon–carbon triple bond in organic molecules has no particular advantages over a similar double bond as regards transmission of electronic effects, despite its greater degree of unsaturation and shorter length.

The coefficient π' for system (I) with M = $-C_6H_4-$ (the *p*-terphenyl system) (Table 3) has the smallest value (0.31), which is consistent with the greatest length of the above bridge. As already mentioned, it is equal to π' for the biphenyl system relative to the benzene system (Table 1).

Data on the transmission of electronic effects in a series of bicyclic systems containing the charged bridges $-\overset{+}{N}(CH_3)=CH-$ and $-CH=\overset{+}{N}(CH_3)-$ (Table 3) require special consideration. Here the π' are significantly greater than unity (1.94 and 3.23 respectively), while the transmission coefficients for the analogous uncharged bridges —CH=N— and —N=CH— are small and virtually equal to the values for other diatomic bridges with a double bond (Table 3). The sharp increase in the transmission efficiency of azomethine bridges following the quaternisation of their nitrogen (by a factor of 4–5) was initially explained[110,111] by a transition from the non-coplanar structure of the Schiff bases, due to the competing interaction of the π electrons of one of the benzene rings both with the double bond and with the lone electron pair of the nitrogen[119–122], to the coplanar structure in the case of the charged bridges, where the above competition does not occur and the benzene ring is conjugated only with the double bond. However, this fact hardly plays a decisive role because in the stilbene, tolane, and azobenzene systems, where the conditions for conjugation are better than in the systems considered here (in the latter there is no steric interaction of the *N*-methyl group with the *ortho*-hydrogen atoms of the benzene ring), the transmission efficiency is virtually the same as in the benzylidene anil systems (cf. the values of π' in Table 3).

The enhancement of the electronic interaction of the substituent with the reaction centre in systems (I) containing unsaturated two-unit bridges relative to system (II) was also observed by Frankovskii and coworkers, who investigated the acidity of the corresponding phenol derivatives (Table 4).

The phenomenon of enhanced transmission efficiency ($\pi' > 1.0$) was observed for the first time in a study of bicyclic systems containing bridge heteroatoms (see the next Section). We shall therefore return somewhat later to the explanation of the "anomalously" high transmission efficiency (Tables 3 and 4). However, here one should note that the introduction of substituents (OH or Cl) into phenol derivatives (Table 4) in the 2- or 2′-position relative to the bridge unit, which influence the steric structure of these compounds, leads to an increase of transmission efficiency. This is manifested particularly

clearly in derivatives of 2,4-dihydroxyazobenzene, where the system becomes more coplanar as a result of the formation of an intramolecular hydrogen bond[50,124,125] and yet another pathway for the transmission of the influence of the substituent on the activity of the reaction centre appears:

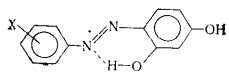

Table 4. Transmission coefficients in the azobenzene system [R and R′ are the substituents in X – (2′-R′) $-C_6H_3-N=N-C_6H_3-$(2-R)–OH-4].

No.	Reaction series	System (II)	R=R′=H		R=H, R′=Cl		R=OH, R′=H	
		ρ_{st}	ρ	π'	ρ	π'	ρ	π'
1	ArOH ⇄ ArO^- + H^+; 20°, 60% EtOH–H_2O [48,49,123–125]	0.81	0.84	1.03	0.93	1.15	2.18	2.68
2	ArOH ⇄ ArO^- + H^+; 20°, 60% dioxan-water [48,49,123,124]	0.76	0.93	1.22	0.98	1.28	1.89	2.48
3	ArOH ⇄ ArO^- + H^+; 20°, 60% acetone-water [50]	0.99	0.91	0.92			2.28	2.31
		π'_{av}	1.06±0.09		1.22±0.07		2.49±0.12	

It is interesting to compare the transmission efficiency data in Tables 3 and 4 with the results obtained in studies of the NMR spectra of a series of analogous compounds.

Table 5. Transmission coefficients estimated with the aid of NMR for systems (I) with bridges containing multiple bonds

No.	Bridge M in (I)	Y=^{19}F [86,103]			Y=^{19}F [87]	Y=OH [50,80]
		π'_I	π'_R	n^a	π'	π'
1	—CH=CH—	0.67±0.02	0.67±0.01	6	0.74[b]	—
2	—N=CH—	0.63±0.01	0.68±0.01	9	—	—
3	—CH=N—	0.63±0.02	0.64±0.01	9	—	—
4	—N=N—	0.91±0.02	0.88±0.01	3	—	0.60[c]
5	$-CH=\overset{+}{N}H-$	1.08[d]	0.62[d]	1	—	—
6	$-\overset{+}{N}H=CH-$	1.47[d]	0.98[d]	1	—	—

[a]The number of solvents in which compounds of types (I) and (II) were investigated (average values of π' are quoted for $n > 1$). [b]Estimated by a direct comparison of the values of Δδ. [c]The chemical shift of the hydroxyl protons were measured and compared. [d]Measurements for compounds of types (I) and (II) were made in FSO_3H and CH_3OH respectively.

Table 5 shows that the transmission efficiency of the system with the –N=N– bridge (No. 4), which has been estimated from the chemical shifts of the hydroxyl protons, agrees well with the efficiency determined from different chemical data (Table 3). On the other hand, the ability of the above bridge to transmit electronic effects determined from the ^{19}F chemical shifts proved to be higher by a factor of 1.5 and its value approached that in Table 4. Hence it follows that the transmission efficiency of the bridge system depends significantly on the nature of the functional centre. The reasons for this will be discussed a little later.

Comparison of the data in Table 5 for the transmission efficiencies of systems (I) with different bridge units, estimated with the aid of the π'_I (for Y = ^{19}F), leads to the conclusion that the efficiency increases steadily on passing from the –CH=CH–, –CH=N–, and –N=CH– bridges, where it does not differ significantly from the value determined for other reaction series (Table 3), to the –N=N–, –CH=NH–, and –NH=CH– bridges. The series based on the transmission efficiency (the bridges are indicated) $-\overset{+}{C}H=CH- \simeq -CH=N- \simeq -N=CH- < -N=N- < -CH=\overset{+}{N}- < =\overset{+}{N}=CH-$ agrees well with the series found from the dissociation data for the corresponding hydroxy-derivatives (No. 6 in Table 3 and Table 4).

IV. SYSTEMS WITH BRIDGE HETEROATOMS CAPABLE OF ELECTRON DONOR CONJUGATION

1. The Positive Bridge Effect (PBE)

In studies on the transmission of electronic effects in a series of systems (I) with bridge heteroatoms on the basis of acylation reactions of the corresponding amino-derivatives (Y = NH_2), the above property was initially estimated in terms of the value of f, [21,126] which is equal to the ratio of the rate constants for the unsubstituted amine and its nitro-derivative (X = H or NO_2). The results (Table 6) show that the introduction of a bridge heteroatom with lone electron pairs between two benzene rings (Nos. 2–5) can not only weaken the electron influence of the substituent on the functional activity of the reaction centre relative to the biphenyl system without a bridge (No. 1) but can also significantly increase it. This phenomenon has been called the positive bridge effect (PBE)[129].

Table 6. The factors f (at 25°C) and ΔpK_a for systems (I) with bridge heteroatoms.

No.	Bridge M in (I)	f_{PNBC}*	f_{PC}	ΔpK_a [48]
1	— (biphenyl)	10.6[91]	13.6[22]	0.54[a]
2	—O—	12.1[127]	15.8[127]	—
3	—S—	23.8[128]	30.7[128]	0.81[a]
4	—Se—	—	24.7[21]	—
5	—NH—	—	43.3[106]	0.82[a]

[a]The difference for X = H and NO_2 is quoted.

*p-nitrobenzoyl chloride (Ed. of Translation).

The first publications dealing with the manifestation of PBE [21,126,129,130] aroused a lively discussion [49,131–138], since they conflicted with the view, established at the time, that the introduction of any bridge unit between a substituent and the reaction centre must lead to the weakening of the electronic interactions between them. Furthermore, the above phenomenon was initially observed

Table 7. Transmission coefficients in systems (I) with bridge heteroatoms (M).

No.	Reaction series	System (II)	M=—O—		M=—Se—		M=—S—		M=—NH—		M=—N(CH₃)—	
		ρ^0_{st}	ρ^0	π'	ρ^0	π'	ρ^0	π'	ρ^0	π'	ρ^0	π'
1	$ArNH_2 + 2,4,6\text{-}(NO_2)_3C_6H_2Cl \rightarrow 2,4,6\text{-}(NO_2)_3C_6H_2NHAr + HCl$; 25°, C_6H_6[34,128,129]	−1.56	−1.64[a]	1.05	−1.91[a]	1.23	−1.96	1.26	−2.15	1.38	−2.82	1.81
2	$ArNH_2 + 4\text{-}NO_2C_6H_4COCl \rightarrow 4\text{-}NO_2C_6H_4CONHAr + HCl$; 25°, C_6H_6[104,127]	−1.40	−1.48[a]	1.06	—	—	−1.88[a]	1.34	—	—	—	—
3	$ArNH_2 + C_6H_5COCl \rightarrow C_6H_5CONHAr + HCl$; 25°, C_6H_6[34]	−1.07	—	—	—	—	−1.70[b]	1.59	−1.92	1.79	−2.22[c]	2.07
4	$ArNH_2 + 4\text{-}NO_2C_6H_4SO_2Br \rightarrow 4\text{-}NO_2C_6H_4SO_2NHAr + HBr$; 25°, $C_6H_5NO_2$[41]	−1.44	—	—	—	—	−1.48	1.03	−1.67	1.16	−2.17	1.49
5	$Ar\overset{+}{N}H_3 \rightleftarrows ArNH_2 + H^+$; 25°, H_2O[48,139]	0.89	1.12[d]	1.26	—	—	1.13	1.27	1.12	1.26	1.40	1.57
6	$Ar\overset{+}{N}H_3 \rightleftarrows ArNH_2 + H^+$; 20°, 50% EtOH—$H_2O$[50,60,135]	0.98	0.92	0.94	—	—	—	—	—	—	—	—
7	$Ar\overset{+}{N}H_3 \rightleftarrows ArNH_2 + H^+$; 25°, CH_3NO_2[140]	0.92[d]	0.79[d]	0.86	—	—	1.28[d]	1.39	1.17[d]	1.26	—	—
8	$ArCOCl + C_6H_5NH_2 \rightarrow ArCONHC_6H_5 + HCl$; 35°, C_6H_6[141,142]	0.32[e]	0.37	1.16	—	—	—	—	—	—	—	—
9	$HON_2ArN_2OH \rightleftarrows HON_2ArN_2O^- + H^+ \rightleftarrows {}^-ON_2ArN_2O^- + 2H^+$; 18°, H_2O[93]	1.73[f]	1.83[f]	1.06	—	—	2.12[f]	1.23	—	—	—	—
			π'_{av}	1.06±0.05		1.23		1.30±0.06		1.37±0.11		1.73±0.13

[a], [b], [c], [d] Determined from two points for X = H and NO_2 (a), H and NH_2 (b), NH_2 and NO_2 (c), or NH_2 and $\overset{+}{N}H_3$ (d). [e] ρ^0_{st} was estimated from ρ^0 for benzene derivatives and the coefficient π'_{av} in Table 1. [f] The difference $pK_1 - pK_2$ is quoted.

only for certain properties (nucleophilic reactivity and basicity) of bridged amino-compounds (Table 6) and was not confirmed when other characteristics of the same substances (for example ultraviolet and Raman spectra) were considered[132,133]. However, it was found subsequently that an enhanced transmission efficiency is observed not only for the bridges listed in Table 6 but also for others (Table 4 and 5) when a large number of compounds (I) are investigated.

Table 7 (Nos. 1–7) presents data on the ability of amino-compounds to transmit electronic effects estimated from the values of ρ^0. The relations governing the variation of π'_{av} thus obtained agree well with the results in Table 6. As in the previous case, the maximum transmission of electronic influences is observed for diphenylamine derivatives. On passing from the biphenyl system to methyldiphenylamine, the sensitivity of the reaction centre to the influence of the substituent increases almost by a factor of two ($\pi'_{av} = 1.73 \pm 0.13$). The systems can be arranged in the following sequence (the bridges are indicated) in terms of their ability to transmit electronic effects: $-N(CH_3)- > -NH- > -S- > -Se- > -O-$. This is consistent (see below) with the ability of the above bridge groups to be involved in electron donor conjugation (p,π interaction).

2. The Nature and Mechanism of the Manifestation of PBE

Together with the increase of transmission efficiency of systems (I) with increase of the electron-donating capacity of the bridge heteroatom[143], mentioned above, the fact that the reactivity of these compounds correlates better with the σ^0,[43,140,143–145] characterising the influence of the substituted phenyl group $X-C_6H_4$, than with the Hammett constants σ is of great importance. On this basis, one may conclude that PBE is due to a combined transmission of the electronic influence, namely simultaneously via the inductive mechanism from one ring to the other and via the mechanism based on the conjugation of the bridge heteroatom with each benzene ring. This conjugation should depend on the inductive effect of the substituted phenyl group. The possibility of a change in the conjugation effects of various groups under the influence of the inductive effects of the substituents attached to them has been confirmed by numerous linear correlations between quantities characterising these effects (Zhdanov and Minkin[6], p. 375)[81,146–150].

Some information about the nature of the conjugation of the bridge heteroatom with the benzene rings in compounds (I) can be obtained by examining their geometrical structures. The molecules of these compounds are nonlinear, since the valence angles at the bridge heteroatom are much smaller than 180°[151–155] and, in consequence of their mutual repulsion, the *ortho*-hydrogen atoms in the benzene rings move apart, forming a dihedral angle φ. Their separation can be achieved in two ways[156,157]: (1) both rings are rotated relative to the C–M–C plane by the same angle $\varphi/2$; (2) one of the rings lies in this plane, while the other deviates from it by an angle φ. The problem of which situation actually obtains still remains open. In many instances[152,153,158–161] the first version appears to be preferred. Certain properties of symmetrical bridged bicyclic compounds calculated on this hypothesis agree fairly well with experimental data[159–161].

At the same time interest has been aroused by studies where it was concluded on the basis of an investigation of microwave[156], infrared, and Raman spectra[157] and dipole moments[156,162,163] that the two rings are equivalent in phenyl ether, diphenyl sulphide (and possibly diphenylamine[156], and their derivatives, i.e. that the second situation applies. It is natural to suppose that under these conditions the bridge heteroatoms can be preferentially conjugated first with one and then with the other

benzene ring and that this transition should be fairly rapid. Therefore methods where the duration of the measurement is longer than the lifetime of one of these states will yield averaged results [164], apparently indicating the equivalence of the conjugation of the bridge atom with the benzene rings. These methods include primarily electron and X-ray diffraction measurements [151]. On the other hand, in those cases where the duration of the measurement of the properties of the substance is shorter than the lifetime of the above molecular "species" the results must indicate their existence, which is consistent with certain spectroscopic data [156,157,165,166].

The satisfactory correlation of the reactivities of various bridged compounds with the σ^0 (Table 7) indicates the absence of a direct conjugation between the substituent and the reaction centre in the compounds. On the other hand, the conjugation in (I) between M and X and between M and Y is quite possible. Therefore the results in Table 7 agree best with the view that in systems (I) the bridge heteroatom is not conjugated simultaneously with both benzene rings.

Table 8.

No.	Bridge M in (I)	Reaction[a] of Compound Ar-NH_2	α	σ_R^{+} [7,34] p-CH_3—M—	α—α_0
1	—(biphenyl)	interaction with PC	0.47	—0.151	0.13
		" with BC	0.44	—	0.40
		" with PNBSB	0.62	—	0.28
		basicity	0.40	—	0.06
2	—CH_2—	interaction with PC	0.34	—0.200	0.21
		" with BC	0.24	—	0.11
		" with PNBSB	0.14	—	0.01
		basicity	0.35	—	0.22
3	—O—	interaction with PC	0.64	—0.604	0.51
		basicity	0.66	—	0.53
4	—S—	interaction with PC	0.81	—0.841	0.68
		" with BC	1.12	—	0.99
		" with PNBSB	0.80	—	0.67
		basicity	0.67	—	0.54
5	—NH—	interaction with PC	0.90	—1.09	0.77
		" with BC	1.28	—	1.15
		" with PNBSP	0.91	—	0.78
		basicity	0.66	—	0.53
6	—N (CH_3)—	interaction with PC	1.21	—1.26	1.08
		" with BC	1.49	—	1.36
		" with PNBSP	1.22	—	1.09
		basicity	0.85	—	0.72

[a]Abbreviations: PC = picryl chloride; BC = benzoyl chloride; PNBSB = p-nitrobenzenesulphonyl bromide.

Thus the manifestation of PBE in bridged amino-compounds is to a large extent due to the ability of the unshared electrons of the heteroatom to enter into electron-donor conjugation with the electronic system of the benzene rings. The constants σ_R^+ (Table 8), which reflect the ability of the p-CH_3-M group to enter into electron-donor conjugation with substituents R via the benzene ring, can be used as quantitative characteristics.

Fig. 1 shows that, for systems with single-unit bridges, there is a definite relation (with a correlation coefficient $r = 0.97$) between their transmission coefficient π'_{av} and σ_R^+. It is interesting to note that the point corresponding to the CH_2 group, where there are no unshared p electrons, also fits satisfactorily on the overall straight line. This most probably indicates that the above bridges interact similarly with the benzene rings in compounds (I). The σ, π conjugation of the methylene group can probably play a role, albeit to a much smaller extent, analogous to that of the p, π conjugation in systems with heteroatoms. The point corresponding to the sulphide bridge in Fig. 1 also fits on the overall straight line, despite the fact that the sulphur atom has vacant d orbitals, which may be involved in conjugation [167-173]. In this case it is probable that this property of the sulphur atom is hardly manifested or contributes in any way to σ_R^+ for the CH_3–S– group.

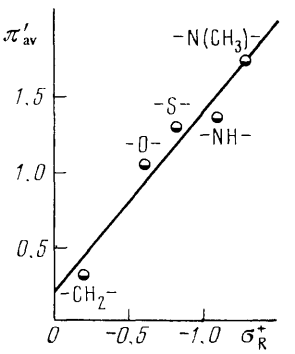

Figure 1. Variation of π'_{av} (Tables 2 and 7) for systems (I) with σ_R^+ (Table 8).

Taking into account the combined transmission of electronic influences in bridged systems, the observed value of ρ^0 for such systems should be linked with the transmission efficiency ρ_1^0 of the monocyclic system (for the same functional group and reaction conditions) by the relation (Palm [7], p. 231)

$$\rho^0 = \rho_1^0 (Z_p^* Z_M^* + \alpha Z_p^R). \qquad (2)$$

This equation reflects quantitatively the fact that the influence of the substituent in systems (I) with PBE is transmitted via both the inductive ($\rho_1^0 Z_p^* Z_M^*$) and conjugation ($\rho_1^0 \alpha Z_p^R$) mechanisms. The quantities Z_p^* and Z_M^* characterise the transmission of the inductive effect by the p-phenylene system and the M bridge, Z_p^R characterises the transmission of the conjugation effect by the p-phenylene system, and α is a measure of the change in the effect of the conjugation of the bridge group with the benzene rings due to the inductive effect of the substituent in the given reaction series.

The quantity ρ_1^0 can be obtained from the reactivities [34,35,44,174] of benzene derivatives by the equation

$$\lg k = \lg k_0 + \rho_1^0 \sigma^0 + \rho_R^+ \sigma_R^+ + \rho_R^- \sigma_R^-, \qquad (3)$$

where ρ_R^+ and ρ_R^- are constants characterising the sensitivity of the reaction series to the conjugation effect of the substituents of the type +R and –R, while $\sigma_R^+ = \sigma^+ - \sigma^0$ and $\sigma_R^- = \sigma^- - \sigma^0$.

The validity of Eqn. (2) was demonstrated using four reaction series for which the required values of ρ^0 (Table 7, Nos. 1 and 3–5) and ρ_1^0 (Table 1, Nos. 6, 8, 10, and 11) are available. Here it is important to stress that in the case of the corresponding monocyclic compounds (aniline derivatives) the effect of the electron-donor conjugation of the substituents ($|\rho_R^+| \gg 0$) [34,35,44] is shown to quite

an appreciable extent for all these series. The values of α calculated for single-unit bridge groups‡, subject to the condition that $Z_p^* = 0.11$, $Z_p^R = 0.43$, [175] and $Z_M^* = 0.40$ (Palm[7], p. 231), are listed in Table 8, which includes also the analogous data for the diphenylmethane system (calculated from the results of Table 2) and the non-bridged biphenyl system ($Z_M^* = 1.00$ according to the data in Table 1).

The α for single-unit bridges increase steadily with increasing capacity of the bridge groups for electron-donor conjugation. However, for a direct comparison of these quantities with the σ_R^+, it is necessary to subtract from them the constant α_0, which is due to the presence in the σ^0 of a resonance component equal to 0.145 σ^* (Palm[7], p. 236). The quantity $\alpha_0 = 0.145 Z_M^*/Z_p^R$ has a numerical value of 0.34 for systems (II) and 0.13 for systems (I) with single-unit bridges.

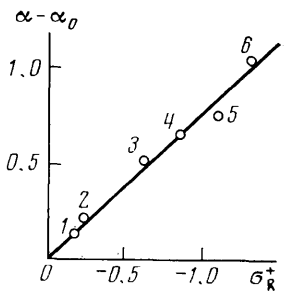

Figure 2. Variation of $\alpha - \alpha_0$ with σ_R^+ ($r = 0.99$) for the reactions of amines [Y = NH_3 in (I)] with picryl chloride. The symbols are numbered as in Table 8.

Comparison of the differences $\alpha - \alpha_0$ with the σ_R^+ (Table 8) shows that, for all the reaction series considered, there are linear relations (see the example in Fig. 2) which pass through the origin of coordinates, i.e. the relation given by the equation

$$\alpha - \alpha_0 = \beta\sigma_R^+. \qquad (4)$$

holds. It is noteworthy that the quantity $\alpha - \alpha_0$ for system (II) is positive (Table 8, No. 1) and the corresponding point in Fig. 2 fits satisfactorily on the common straight line for bridged systems. It is as yet difficult to explain this finding. However, the hypothesis that the inductive effect of the substituent influences the degree of conjugation (in the present instance the electron-donor conjugation) between the benzene rings does not lack justification.

‡It is assumed to a first approximation that the ability of the bridges to transmit electronic effects by the inductive mechanism is independent of their nature (Palm[7], p. 233). This conflicts with data on the correlation of the NMR spectra of fluoro-derivatives (Tables 5, 10, 11), for which the values of π'_I vary appreciably as a function of the nature of the bridge. The latter is probably due to the fact that, when the ^{19}F chemical shifts for such compounds are correlated, ρ_I is a more complex function than would appear from a formal examination of Eqn. (1).

Thus the results can serve as a quantitative confirmation of the above hypothesis that the influence of substituents on the functional activity of the reaction centre in type (I) amino-compounds is transmitted both by the inductive mechanism and by the mechanism based on electron-donor conjugation of the bridge heteroatom with each benzene ring. Here it is particularly significant that in the latter case the relative change in conjugation[176] under the influence of the substituent, defined by the product $\beta\sigma_R^+$ in Eqn. (4), and not its absolute magnitude, plays the principal role.

3. The Limits of the Manifestation of PBE

Since the capacity of the bridge group for electron-donor conjugation is not limitless, it follows that, as the electron-accepting properties of the substituents X in (I) become more pronounced, a situation may arise where this capacity has been completely exhausted. Subsequently the electronic influence on the reaction centre by the ring with the substituent must be transmitted preferentially via the inductive mechanism. In this case the plot of lg k against σ^0 will consist of two linear sections: one with a larger slope, where PBE is manifested, and one with a smaller slope, where there is no PBE. The abscissa (σ^0) of the break point may be designated by σ_{cr}^0 (Palm[7], p. 237).

The reactivities of 4-aminodiphenylamine with several electron-accepting substituents in the benzene ring without the reaction centre have been examined from this standpoint[177,178]. The findings agree qualitatively with the above considerations, but are somewhat complicated by the possibility of forming an intramolecular hydrogen bond between the imino-bridge and the *ortho*-substituent (nitro-group)[179-181].

More definite data were obtained in a study of the reactivities of triphenylamine derivatives with various substituents in the 4′- and 4″-positions[178,182,183]. The corresponding correlation graph, based on basicity data (Fig. 3*A*), agrees fully with the prediction. This suggests that in these systems the capacity of the bridge nitrogen for conjugation is already exhausted following the introduction of one nitro-group. On the other hand, in the reactions of these amines with *p*-nitrobenzenesulphonyl bromide (PNBSB) this situation is attained following the introduction of two nitro-groups (Fig. 3*B*), while the reaction with picryl chloride could not be achieved in the experimental $\Sigma\sigma^0$ range (Fig. 3*C*).

Comparison of the ρ^0 for different sections of the correlation graph in Fig. 3 with the analogous values for aminobiphenyl derivatives [system (II)] in the same reaction series makes it possible to estimate the ability of the bridge group to transmit electronic effects in its various states. In those cases where the capacity of the bridge nitrogen atom for conjugation has not been fully exhausted (the left-hand branches *A* and *B* and straight line *C*), PBE is clearly manifested (the π' are respectively 1.17, 1.29 and 1.24)[34,41,182]. After σ_{cr}^0 has been reached (the right-hand branch *A*), the transmission coefficient of the nitrogen atom ($\pi' = 0.21$) [178] is much smaller than for the methylene unit in system (I) (Table 2). Furthermore, it is smaller by a factor of two than the coefficient defining the capacity of this unit for transmission of electronic effects by the inductive mechanism alone (0.388). The extremely low transmission coefficient obtained for the electron-deficient nitrogen atom agrees satisfactorily

with π' for the positively charged nitrogen atom in *N*-protonated derivatives of *N*-arylglycines (0.22) [183,184] and the nitrogen atom in the amide group (0.23) [185].

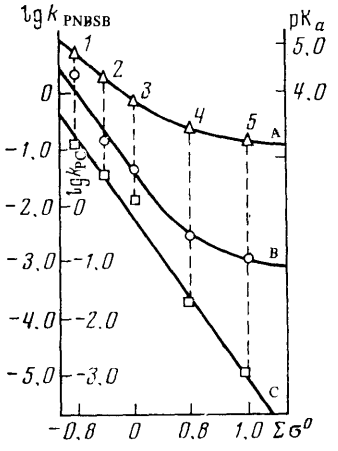

Figure 3. Variation with $\Sigma\sigma^0$ of pK_a (A) for triphenylamine derivatives [4′-X-C_6H_4-N(Ar)-C_6H_4-NH_2-4] in 45% aqueous dioxan [162] and of lg *k* for the reactions of these amines with nitrobenzenesulphonyl bromide (B) in nitrobenzene and with picryl chloride (C) in benzene [166] at 25°C; X and Ar in the formula: 1) 4′-NH_2, 4″-NH_2. .C_6H_4; 2) 4′-NH_2, C_6H_5; 3) H, C_6H_5; 4) H, 4″-$NO_2C_6H_4$; 5) 4′-NO_2, 4″-$NO_2C_6H_4$.

All these findings show that PBE can be manifested only in those cases where the reaction series investigated (for benzene derivatives as an example) is sufficiently sensitive to electron-donor conjugation [ρ_R^+ in Eqn. (3) differs significantly from zero] and the bridge group M in compounds (I) has unshared electrons capable of being involved in such conjugation.

o0o

On the basis of the principles formulated above, it is interesting to examine data describing the ability of systems (I) with bridge heteroatoms to transmit electronic effects, which have been obtained from other reaction series (Y ≠ NH_2). Since the reaction of benzoyl chloride derivatives with aniline is fairly sensitive to the electron-donor conjugation of substituents [186], the manifestation of PBE in the phenyl ether system for Series No. 8 (Table 7) becomes quite understandable. For the same reason (high sensitivity to the above conjugation [137], an enhanced transmission efficiency of systems (I) with M = –O– and –S– is observed in Series No. 9 (Table 7).

It is interesting that, in a study of the transmission efficiencies of systems (I) on the basis of acid dissociation data (Y = OH), Frankovskii and coworkers [49,50,135–137] concluded that the bridge heteroatoms have an insulating influence. At the same time their results (Table 9) show that in this case the transmission efficiency increases in the sequence (the bridges M are indicated) –O– < –S– < –NH–, while in the case where M = –NH– it virtually coincides with that of system (II). The parallel variation of the π' in Table 9 and the σ_R^+ for CH_3–M groups (Table 8) suggests that in this case the capacity of the bridge atom for electron-donor conjugation plays a significant role. Since the acid dissociation of phenols is almost insensitive to such conjugation ($\rho_R^+ = 0$) [44], it follows that the higher values of π'_{av} in Table 9 compared with the coefficient giving the transmission efficiency for a single-atom bridge solely by the inductive effect (0.388) is due to the conjugation of the bridge heteroatom with the benzene ring containing this substituent and not with the ring in which the reaction centre is located. This constitutes direct confirmation that the manifestation of PBE requires that the bridge heteroatomic group should enter into electron-donor conjugation with each benzene ring.

Table 9. Transmission coefficients in systems (I) (Y = OH) with bridge heteroatoms.

No.	Reaction series	System (II)	M=—O—		M=—S—		M=—NH—	
		ρ_{st}	ρ	π'	ρ	π'	ρ	π'
1	ArOH ⇄ ArO^- + H^+; 20°, 60% EtOH–H_2O [49,50,135,137]	0.81	0.39	0.48	0.55 0.57[a]	0.68 0.70	0.77	0.95
2	ArOH ⇄ ArO^- + H^+; 20°, 60% dioxan-water [135–137]	0.76	0.29	0.38	0.57 0.76[a]	0.75 1.00	0.73	0.96
3	ArOH ⇄ ArO^- + H^+; 20°, 60% acetone-water [50]	0.99	0.44	0.44	0.59 0.72[a]	0.60 0.73	0.88	0.89
		π'_{av}	0.43±0.03		0.68±0.04 0.81±0.10[a]		0.93±0.02	

[a] The X-(2′-Cl)-C_6H_3-S-C_6H_4-Y-4 system is considered.

Comparison of the chemical shifts (Table 10) in the NMR spectra of compounds of type (I) shows that, as expected, there is no full correspondence between the series being compared. For fluorobenzene derivatives, where the chemical shift depends significantly on the effect of the electron-donor conjugation of the substituents (Zhdanov and Minkin [6], p. 375), the introduction of bridge heteroatoms between the benzene rings (Table 10, Nos. 1–3) leads to an increased influence of the substituent on the given property, i.e. PBE is clearly manifested in this instance. On the other hand, measurements of the chemical shifts due to the proton in the hydroxy-group have shown that, although the ability of bridge groups to transmit electronic effects does increase on passing from oxygen to nitrogen, it does not exceed that of system (II). As for the acid dissociation of the above compounds (Table 9), the absence of PBE in this case is caused by the insensitivity of the proton chemical shifts in the series of phenol derivatives to the electron-donor conjugation of substituents [78].

An enhanced transmission coefficient of the heteroatom ($\pi' > 1.0$) has been observed in a study of NMR spectra also in other series where the bridge heteroatom was incorporated between two π-electron systems (for example a benzene ring and a vinyl group) [171–173,188]. The transmission coefficient of the system with M = –S– then proved to be greater than for M = –O–.

The full analogy between the results obtained in measurements of the reactivities of amino-compounds

(Table 7) and the ^{19}F chemical shifts (Table 10) for compounds of type (I) with bridge heteroatoms suggests that Eqns. (2) and (4) are applicable to the latter case. Indeed, Fig. 4 shows that the relation between the α calculated from the data in Table 10 and the σ_R^+ (Table 8) is described by a straight line passing through the coordinate origin, in accordance with Eqn. (4). The point for diphenylmethane fits on the same line, as in Fig. 2. However, the point for system (II) deviates appreciably from the general line, which is probably due to the characteristic features of the transmission of electronic influences in the series of fluoro-derivatives (see below).

Table 10. Transmission coefficients estimated from NMR spectra in systems (I) with bridge heteroatoms.

No.	Bridge M in (I)	Y=^{19}F[86,103]			Y=^{19}F[87]	Y=OH[50,80]
		π_I'	π_R'	n[a]	π'	π'
1	—O—	1.00±0.01	1.08±0.01	9	1.10[b]	0.52[c]
2	—S—	1.21±0.01	1.42±0.01	9	1.51[b]	—
3	—NH—	1.50	1.84	1	—	0.76[c]
4	—$\bar{C}$Ph—	3.34	2.86	1	—	—
5	—N=$\bar{C}$—	2.74	1.80	1	—	—

[a]The number of solvents in which bridged compounds of types (I) and (II) were investigated. [b]Estimated by a direct comparison of the values of $\Delta\delta$. [c]The chemical shifts of the hydroxyl proton were measured and compared.

The highest transmission coefficient in the series of fluoro-derivatives has been observed for the $-\bar{C}$Ph– bridge (Table 10, No. 4) bearing an integral negative charge, which maximises its capacity for electron-donor conjugation. An enhanced transmission coefficient has also been observed for the $-N=\bar{C}-$ bridge (No. 5) whose capacity for conjugation should be fairly high.

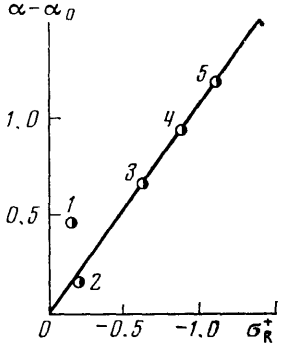

Figure 4. Variation of $\alpha - \alpha_0$ with σ_R^+ ($r = 0.99$) for systems (I) with M = $-CH_2-$ (*2*), –O– (*3*), –S– (*4*), and –NH– (*5*) and for system (π) (*1*) on the basis of NMR (Y = ^{19}F) [86,103].

Analysis of the corresponding infrared spectroscopic data for a series of benzoic acid derivatives (the C=O stretching vibration frequencies) indicates their high sensitivity to electron-donor conjugation by the substituents ($\rho_R^+ \gg 0$). This is precisely why PBE was observed in studies by this method of compounds of type (I) with Y = $COOCH_3$ and M = –O–. [145,189]

PBE was also observed in a study of the stretching vibration frequencies of N – H in compounds (I) with Y = NH_2 in the presence of bridges such as –O–, –S–, –NH–, and $-N(CH_3)-$. [43] This is fully consistent with the above considerations, since the frequencies for aniline derivatives [190] depend significantly on the capacity of the substituents for electron-donor conjugation.

Thus data derived from NMR spectra (Table 10) and infrared spectra of compounds of type (I) fully confirm the conclusions reached about the mechanisms and characteristics of the manifestation of PBE obtained in studies on the reactivities of the corresponding compounds (Tables 7 and 9).

V. SYSTEMS WITH SINGLE-UNIT BRIDGE GROUPS CAPABLE OF ELECTRON-ACCEPTOR CONJUGATION

The data examined above concerning the manifestation of PBE refer mainly to systems (I) where the bridge consists of heteroatoms capable of electron-donor conjugation. It is reasonable to suppose that, in those cases where the reaction series is characterised by a high sensitivity to the electron-accepting effect of the substituents ($|\rho_R^-| \gg 0$), PBE can also be manifested in systems (I) with bridge groups capable of electron-acceptor conjugation.

For reactions involving substituted anilines, ρ_R^- in Eqn. (3) is fairly high. This is in fact why studies on the nucleophilic reactivity of 4'-derivatives of 4-aminobenzophenone [21,191] yielded $\pi'_{av} = 0.91$ (for reactions with *p*-nitrobenzoyl chloride and picryl chloride). This shows that system (I) with M = –CO– hardly differs from system (II) in its ability to transmit electronic effects, i.e. an enhanced transmission efficiency was observed for the first time in bycyclic systems with bridge groups capable of electron-acceptor conjugation.

Subsequently enhanced transmission efficiencies of systems (I) with the above bridge groups were observed in studies of the acid dissociation of the corresponding hydroxy-compounds (Tables 3 and 4) and the NMR spectra of fluoro-derivatives (Table 5). Here it is important to emphasise that in the cases examined PBE is shown only for fairly powerful electron-accepting bridge groups and varies in the sequence $-NR=CH- > -CH=NR- > -N=N-$, i.e. in the same sequence as the electron-accepting capacity of these bridges. For groups with weaker electron-accepting capacities, such as –CH=N–, –N=CH–, –C≡C–, and –CH=CH– (Tables 3–5), the coefficients π' are appreciably less than unity.

These bridges do not show high transmission efficiencies for systems (I) (Tables 3–5), although all the reaction series examined (with the exception of Nos. 7 and 8 in Table 3) are sensitive to electron-acceptor conjugation [when data for benzene derivatives are interpreted in terms of Eqn. (3), the ρ_R^- are non-zero]. This shows that PBE is observed only after the attainment of a specific capacity of the bridge group for electron-acceptor conjugation and when the reaction centre is highly sensitive to such conjugation. This is confirmed also by measurements of the transmission coefficients of systems (I) with M = $-SO_2-$. Whereas according to the dissociation data for 4-hydroxy-derivatives $\pi' = 1.24$ in the

diphenyl sulphone system[50] (i.e. PBE is clearly manifested), the study of the nucleophilic reactivities of the corresponding 4-amino-derivatives with respect to picryl chloride in nitrobenzene showed that $\pi' = 0.68$ (PBE not observed)[192].

Since the NMR spectra of fluorobenzene derivatives are fairly sensitive to both electron-donor and electron-acceptor conjugation (Zhdanov and Minkin[6], p. 375), it is quite reasonable that, in NMR studies of compounds of type (I) (Y = ^{19}F), PBE is observed for both electron-donating (Table 10) and some electron-accepting (Table 5) bridge groups. As already stated, in the latter case, PBE is not observed in all cases but only for the most electron-accepting bridges§. This hypothesis is confirmed particularly clearly by the data in Table 11, where the transmission coefficients for bicyclic systems with single-unit bridges increase steadily as the electron-accepting properties of the bridge group and its capacity for electron-acceptor conjugation become more marked, reaching a maximum value ($\pi'_I = 13.9$) for the powerful acceptor $-\overset{+}{C}(CF_3)-$ (No. 11).

Table 11. Transmission coefficients estimated with the aid of NMR in systems (I) with single-unit electron-accepting bridges.

No.	Bridge M in (I)	Y=^{19}F[86,103]		Y=^{19}F[87]
		π'_I	π'_R	π'
1	$-\overset{CH_2}{\overset{\parallel}{C}}-$	—	—	0.48[a]
2	$-\overset{O}{\overset{\parallel}{C}}-$	0.73	0.59	0.76[a]
3	$-\overset{NH}{\overset{\parallel}{C}}-$	0.82	0.63	—
4	$-\overset{O\cdot BF_3}{\overset{\parallel}{C}}-$	1.82	1.35	—
5	$-\overset{O\cdot BCl_3}{\overset{\parallel}{C}}-$	2.23	1.56	2.44[a]
6	$-\overset{O\cdot BBr_3}{\overset{\parallel}{C}}-$	2.24	1.61	—
7	$-\overset{+}{C}(OH)-$	2.26	1.69	2.72[a]
8	$-\overset{+}{C}Ph-$	3.14	2.40	—
9	$-\overset{+}{C}(CH_3)-$	5.80	4.86	—
10	$-\overset{+}{C}H-$	7.07	5.29	—
11	$-\overset{+}{C}(CF_3)-$	13.9	10.4	—

[a]Estimated by a direct comparison of the values of $\Delta\delta$.

Unfortunately, owing to the lack of $\sigma_{\bar{R}}$ constants, characterising the capacity of the CH_3-M- groups for electron-acceptor conjugation, it was not possible to interpret the data considered in the present section in terms of equations analogous to Eqns. (2) and (4).

It is interesting that the coefficients π'_R calculated from the corresponding ρ_R constants increase in parallel with increase of the π'_I (Tables 5, 10, and 11). The reasons for the observed variation of these constants as the bridge M in (I) is varied are not yet altogether clear. Nevertheless, it is noteworthy that the very appearance of the constants ρ_R, which usually characterise the interaction between the substituent and the functional centre via the conjugation mechanism, can hardly be caused here by this interaction. The point is that the ρ_R are not zero even in series such as p-X-C_6H_4-CH_2-^{19}F, p-X-CH_2-C_6H_4-^{19}F, and p'-X-C_6H_4-CH_2-C_6H_4-^{19}F-p,[103] where such conjugation should not occur.

The above data permit the conclusion that in bridged bicyclic systems of type (I) the electronic interaction between the substituent and the reaction centre can be not only weaker than in the non-bridged biphenyl system (II) but in some cases can also be several times stronger. This enhancement of the interaction, i.e. the positive bridge effect, is manifested distinctly only when the following conditions are observed:

1. The reaction series investigated (Ar–Y) is fairly sensitive for benzene derivatives to electron donor (or electron-acceptor) conjugation, i.e. the constant $\rho_{\overset{+}{R}}$ (or $\rho_{\bar{R}}$) in Eqn. (3) is appreciably different from zero.
2. The bridge group can be involved in the above conjugation, i.e. $\sigma_{\overset{+}{R}}$ (or $\sigma_{\bar{R}}$) for the CH_3-M- group is much smaller (or greater) than zero.
3. The bridge group is conjugated with each benzene ring to an extent which varies as a result of the inductive effect of the substituted ring.

§The deviation of the point for system (II) in Fig. 4 (No. 1) is probably caused by the enhanced transmission efficiency due to the capacity of the benzene ring for electron-acceptor conjugation.

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Silylation of Organic Compounds

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The mechanism of the silylation reaction and the methods of synthesis and properties of silylating agents are discussed together with the silylation of various classes of compounds in relation to the most characteristic substances. The bibliography includes 186 references.

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I. INTRODUCTION

The silylation reaction (particularly the trimethylsilylation reaction) is nowadays widely used in organic synthesis. "Silylation" is usually understood as the introduction of the silyl group in place of a labile hydrogen atom or a metal atom substituting the latter and it is essential that the group thus introduced can be readily removed with reintroduction of active hydrogen.

Silylation makes it possible to modify widely various properties of the starting materials: it alters the reactivity of the products and, in particular, makes it possible to block certain reaction centres, it improves the solubility of compounds in non-polar solvents and increases the volatility of products as the result of the disappearance of hydrogen bonds, thus permitting their analysis and separation by gas–liquid chromatography and mass spectrometry. Finally, in certain cases the stability of the initial substances increases after silylation, for example $(CH_3)_3SiN_3$ is more stable than HN_3.

Pierce's monograph[1] surveys data on the silylation of organic compounds up to 1967. Furthermore, there are a number of reviews dealing with individual aspects of silylation[2-6] and also with the use of silyl derivatives in gas–liquid chromatography[7,8]. However, we believe that, in view of the relative inaccessibility of the majority of the above sources to the Russian reader and also the publication in recent years of many new and interesting data, it is desirable to publish the present review.

II. THE MECHANISM OF THE SILYLATION REACTION

The majority of investigators believe that the silylation reaction is reversible and proceeds via a mechanism involving bimolecular nucleophilic substitution at the silicon atom[1]:

$$HY + R_3SiX \rightleftarrows \overset{\delta-}{Y} \cdots \underset{\displaystyle H \quad R}{\overset{R\ R}{Si}} \cdots \overset{\delta-}{X} \rightleftarrows HX + R_3SiY, \qquad (1)$$

where Y is the nucleophilic component of the molecule of the compound being silylated and X is the group substituted in the silylating compound.

According to another view[9], the silylation reaction proceeds via a many-centre transition state:

$$HY + R_3SiX \rightleftarrows \begin{matrix} R_3Si{-}X \\ \vdots\ \ \vdots \\ Y{-}H \end{matrix} \rightleftarrows R_3Si{-}Y + HX. \qquad (2)$$

In many instances the rate-limiting stage of the reaction is believed to be the protonation of the silylating agent, preceding nucleophilic attack on the silicon atom[10]:

$$HY + R_3SiX \overset{\text{slow}}{\rightleftharpoons} [R_3SiX \cdots H]^+ \rightarrow \xrightarrow{Y^- \text{ or } HY} R_3SiY + HX. \qquad (3)$$

There are two criteria whereby it is possible to choose between particular silylation mechanisms. One of these is based on a kinetic study in which the order of the reaction with respect to the reactants and the rate-limiting stage are determined. The second is based on the study of silylation by agents containing an asymmetric silicon atom. This procedure for elucidating the mechanism has become possible as a result of detailed studies by Sommer[11], who obtained a set of optically active compounds with an asymmetric silicon atom and determined their true configurations.

The "optical" criterion makes it possible to investigate directly the mechanism of the substitution stage at the silicon atom even if it is not rate-determining. Sommer suggests[11] that silicon is capable of giving rise to transition structures in the silylation reaction as a result of the involvement of its vacant *d* orbitals. Three possible versions are considered.

1. The inversion of the optical configuration at the silicon atom (here and henceforth we shall designate this process, following Sommer[11], as S_N2–Si). In this case the group X is replaced by Y via a bimolecular mechanism and the transition state has the geometry of a trigonal bipyramid (Fig. 1).

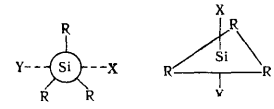


Figure 1. Geometry of the transition state in an S_N2–Si reaction.

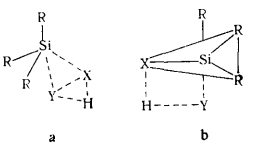
2. The retention of the optical configuration at the silicon atom (we shall designate this process by S_Ni–Si)[11]. Here the reaction is also bimolecular but the geometry of the transition state changes. It is either a tetragonal

pyramid (Fig. 2*a*) or a trigonal bipyramid in which the relative positions of X and Y are not the same as in Fig. 1 (Fig. 2*b*).

3. The loss of optical activity. In this case the reaction either proceeds via the S_N1–Si mechanism involving the formation of a planar siliconium cation:

$$R_3Si{-}X \rightleftarrows R_3Si^+ + X^- \overset{HY}{\rightleftarrows} R_3SiY + HX\,,$$

or it proceeds simultaneously via the S_N2–Si and S_Ni–Si mechanisms. Evidently a choice can be made between these two versions kinetically using the order of the reaction with respect to each reactant.



a b

Figure 2. Geometry of the transition state in a S_Ni–Si reaction.

Since the siliconium cation R_3Si^+ is relatively unstable[12], and the silylation reaction is usually carried out in aprotic solvents of low polarity, we believe that "racemisation" is most probably a consequence of a bimolecular reaction mechanism intermediate between S_N2–Si and S_Ni–Si.

1. Reaction Kinetics

It has been shown that in many cases the rate determining stage in the silylation reaction is nucleophilic substitution at the silicon atom. Thus Grubb[13] established that silylation of trimethylsilanol in methanol proceeds with participation of the solvent and is catalysed by acids or bases. It was found that the reaction is of first order with respect to the silanol, chlorotrimethylsilane, and the catalyst. The following reaction mechanism was proposed:

$$(CH_3)_3SiOH + CH_3OH \rightleftarrows (CH_3)_3SiOCH_3 + H_2O\,.$$

Then, in the presence of an acid catalyst we have

$$(CH_3)_3SiOCH_3 + CH_3\overset{+}{O}H_2 \rightleftarrows (CH_3)_3Si\overset{+}{O}CH_3 + CH_3OH,$$

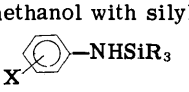
$$(CH_3)_3SiOH + (CH_3)_3Si\overset{+}{O}CH_3 \overset{slow}{\rightleftarrows} \left[(CH_3)_3SiO \cdots \overset{CH_3\ CH_3}{Si} \cdots OCH_3\right] \rightleftarrows$$

$$\rightleftarrows [(CH_3)_3Si]_2O + CH_3\overset{+}{O}H_2\,,$$

and in the presence of a basic catalyst

$$(CH_3)_3SiOH \overset{OH^-}{\rightleftarrows} (CH_3)_3SiO^- + H_2O,$$

$$(CH_3)_3SiO^- + (CH_3)_3SiOCH_3 \overset{slow}{\rightleftarrows} \left[(CH_3)_3SiO \cdots \overset{CH_3\ CH_3}{Si} \cdots OCH_3\right] \rightleftarrows [(CH_3)_3Si]_2O + CH_3O^-.$$

The kinetics of the reaction of methanol with silylamines having the general formula  —NHSiR$_3$

(where X = H, CH_3, OCH_3, C_2H_5, Cl, or F and R = alkyl) have been studied[14]. The reaction was carried out in an excess of methanol in the presence of or absence of acid catalysts. It was shown that it is irreversible and is of first order with respect to silylamine and the catalyst. For substituents X in the *meta*- and *para*-positions, a linear relation was observed between $\lg K = \lg(k_1/k_0)$ and the Hammett constants σ of the substituents (the sensitivity coefficient $\rho = -2.52$). Very rapid deuterium exchange between methanol and the silylamine was observed. Bearing in mind the data concerning the reaction order, the sign and magnitude of the sensitivity coefficient ρ, and the high activation entropy, the authors[14] suggested a mechanism for this process in which the rate-determining stage is the interaction of the protonated silylamine with methanol:

$$\begin{gathered} ArNHSi(iso\text{-}C_3H_7)_3 + (CH_3\overset{+}{O}H_2) \overset{fast}{\rightleftarrows} Ar\overset{+}{N}H_2Si(iso\text{-}C_3H_7)_3 + CH_3OH\,, \\ Ar\overset{+}{N}H_2Si(iso\text{-}C_3H_7)_3 + CH_3OH \rightarrow ArNH_2 + (iso\text{-}C_3H_7)_3Si\overset{+}{O}CH_3\,, \\ \qquad\qquad\qquad\

2. Stereochemistry of the Reaction

The silylation of compounds containing a mobile hydrogen atom with the aid of optically active trialkylhalogenosilanes proceeds as a rule with almost complete inversion of the configuration of the R_3Si fragment[20-25]. The silylation of water and methanol by silylamines[25-27] and the silylation of methanol by alkoxycarbonylsilanes proceed similarly[28]. On the other hand, the interaction of organic acids and HCl with silylamines can proceed both with and without inversion of optical configuration[26,29]†.

Examination of the kinetic and stereochemical data for the silylation reaction shows that it usually proceeds via the S_N2–Si mechanism. The silylating agent can interact in both neutral and protonated forms, the latter being apparently preferable. The silylated compound reacts either as an anion or as a neutral molecule. However, in many instances the silylation reaction proceeds via the S_Ni–Si mechanism or simultaneously via the S_N2–Si and S_Ni–Si mechanisms.

3. Additional Data on the Silylation Mechanism

In addition to the kinetic and stereochemical studies already discussed, it is necessary to consider certain investigations which also provide information about the mechanism of the silylation reaction.

A hypothetical S_Ni–Si mechanism involving a many-centre transition state has been postulated for some reactions. In particular, such a mechanism has been suggested for the silanolysis of silylamines[10]:

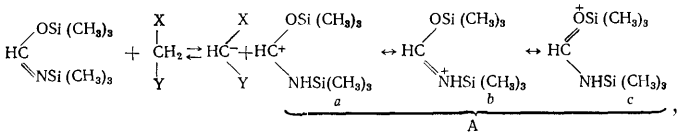
$$R_3SiOH + R'_3SiNR''_2 \rightarrow R_3Si{-}O{-}H \rightarrow R_3SiOSiR'_3 + R''_2NH.$$
$$\vdots$$
$$R'_3Si{-}NR''_2$$

According to Becke-Gochring and Wunsch[30], the interaction of hexamethyldisilazane with compounds containing a mobile hydrogen atom may be accompanied by the formation of an intermediate complex‡:

$$[(CH_3)_3Si]_2NH + HX \rightarrow [(CH_3)_3Si{-}\underset{\uparrow\ \downarrow}{N}HSi(CH_3)_3] \rightarrow (CH_3)_3SiX + [(CH_3)_3SiNH_2],$$
$$X{-}H$$

where X = Cl, OC_2H_5, or OC_6H_5.

In their study of the silylation of weak C–H acids by *N O*-bis(trimethylsilyl) formamide Kentlenner et al.[10] suggested that the silylating agent is initially protonated with formation of an ambident cation A§:



where X = RCO for R = CH_3 or C_6H_5 and Y = $CO_2C_2H_5$, for R = CH_3OCOCH_2 and Y = CO_2CH_3, or for R = C_6H_5 and Y = $COCH_3$ and X = CN for Y = CN, $CO_2C_2H_5$, or CO_2CH_3.

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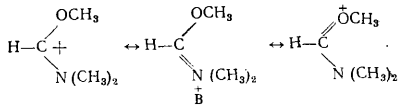
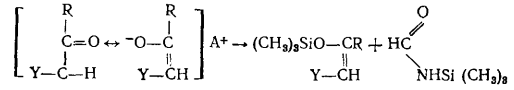
† These results are explained in the next section of this review.

‡ However, the authors do not rule out also other reaction mechanisms.

§ The cation A can be regarded as the silylated analogue of the ambident cation B:[31]

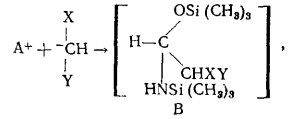


When the anion formed from the C–H acid is capable of tautomerism, the ambident cation A reacts with it in form (*b*) or (*c*), giving rise to an *O*-silylation product:



where Y = $COOC_2H_5$, $COOCH_3$, or $COCH_3$.

When the anion of the C–H acid is incapable of tautomerism, the cation A reacts with this "hard" anion in form (*a*) to form compounds of type C, which are unstable and undergo further reactions:



where X = CN and Y = CN, $COOCH_3$, or $COOC_2H_5$.

Thus several different mechanisms have been proposed for the silylation reaction¶. We believe that this process should not be always treated from the standpoint of any one mechanism, since the reaction mechanism can probably change under the influence of many factors.

4. The Influence of the Nature of the Group X Substituted in the Silylating Agent R_3SiX

Examination of Eqn. (1) shows that the rate of silylation must depend on the properties of the substituent X as the group to be eliminated†. Firstly, it is desirable that X should be capable of delocalising the negative charge arising on it in the transition state. Secondly, the weaker the $(d-p)_\pi$ interaction between the silicon atom and the group X, the greater the ease of nucleophilic attack on the silicon atom and the dissociation of the Si–X bond. In many cases the rate of the silylation reaction depends on the ease of protonation of the compound R_3SiX [Eqn. (3)] and the role of protonation should become more important as X becomes more difficult to eliminate.

Certain ideas about the influence of the nature of the group X on the ease of substitution are provided by the series of conversions deduced by Eaborn[33] and Anderson and Fischer[34] on the basis of studies of the reactions of certain silver salts with triorganosilanes:

$$\rightarrow \text{SiI} \rightarrow (\text{Si})_2\text{S} \rightarrow \text{SiBr} \rightarrow \text{SiH} \rightarrow \text{SiNC} \rightarrow \text{SiCl} \rightarrow \text{SiNCS} \rightarrow \text{SiNCO} \rightarrow$$
$$\rightarrow (\text{Si})_2\text{O}, \text{SiF}.$$

In this series the reactions of the compounds $\rightarrow$SiX with the salt AgY proceed only from left to right.

The most thoroughly investigated silylating agents are compounds with an Si–N bond. These organosilicon derivatives have been arranged in the following sequence in terms of their silylating capacity[1,15]:

$$R_3Si{-}N\begin{matrix}R'\\R''\end{matrix} < R_3SiNR'CONR''R''' \sim R''CONR'SiR_3 < R''C(OSiR_3){=}NSiR_3.$$

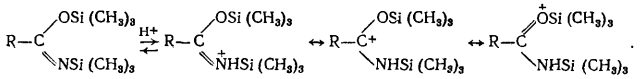
¶ In addition to the foregoing, we may mention that a radical-anion mechanism has been put forward for the silylation of ketones in the presence of an alkali metal[32].

† X must be more electronegative and less nucleophilic than Y in the compound HY being silylated. Otherwise HX must be removed from the reaction sphere in order to shift the equilibrium towards the silylation products.

Silylamines are less effective donors of the trimethylsilyl group than silylated ureas and amides. *NO*-Bis-(trimethylsilyl)amides are the best silylating agents for the majority of compounds to be silylated, among those known at the present time.

The explanation is that, firstly, the introduction of the carbonyl group at the nitrogen atom linked to the silicon atom weakens the $(p - d)_\pi$ interaction between them and facilitates nucleophilic attack on the silicon atom. The introduction of a second trimethylsilyl group into silylated amides weakens still further the double-bond character of the linkage between the silicon atom and the group X to be substituted. Secondly, on passing from silylamines to silylated amides and ureas, there is an increase of the capacity of the group X being eliminated for the delocalisation of the negative charge due to the carbonyl group.

Furthermore, *NO*-bis(trimethylsilyl)amides are more readily protonated than silylamines and silylureas, since the resulting positive charge is more effectively stabilised:



The substituent at the nitrogen atom in the group $-CO-N(X)-Si$ also influences the reactivity of *N*-silylamides.

The study of the methanolysis of *N*-methyl-*N'*phenyl-*NN'*-bis(trimethylsilyl)urea showed that the trimethylsilyl group at the nitrogen atom linked to the more electronegative substituents is more mobile[15]:

$$C_6H_5N[Si(CH_3)_3]CON(CH_3)Si(CH_3)_3 \xrightarrow{CH_3OH} C_6H_5NHCON(CH_3)Si(CH_3)_3.$$

It is noteworthy that the ease of protonating of silylamides depends very markedly on the contribution of the amide formed to the structure of the amide and on the energy barrier between the amide and imide forms (see Section III). A decrease of the barrier and an increase of the content of the form C in the mixture should facilitate the protonation of silylamines (in consequence of the resonance stabilisation of the cation $R-C(OSi<)(\overset{+}{N}HR')$) and hence improve the silylating capacity of these compounds.

In conclusion we shall consider briefly the influence of the group X being substituted in silylating agents with an Si–O bond. Sommer et al.[23] investigated the rate of solvolysis of alkoxy- and acyloxy-silanes R_3SiOR' and $R_3SiOCOR'$. Trialkylacyloxysilanes are more reactive, owing to the greater stabilisation of the charge by the group $(-OCOR')^-$ compared with $(OR')^-$ and the smaller amount of double bond character of the linkage between the silicon atom and the group being substituted in acyloxysilanes compared with alkoxysilanes.

5. The Influence of the Nature of the Compound HY Being Silylated

The silylation mechanism may be also determined by the properties of the compound being silylated. If the compound HY has pronounced nucleophilic properties, then reaction (1) should be favoured. An increase of the acidity of HY with retention of fairly marked nucleophilic properties should lead to a many-centre cyclic transition state, in accordance with Eqn. (2). Under these conditions, when the acidity of HY is of decisive importance, the rate-limiting stage becomes the protonation of the silylating agent [Eqn. (3)].

Hydroxy-compounds are known to be more readily silylated than compounds with an N–H bond[35]. Possibly this is because alcohols are stronger acids than amines. For this reason, they, on the one hand, protonate more readily the silylating agent (see acid catalysis) and, on the other hand, they are themselves more readily deprotonated, the anion RO^- being more nucleophilic than the amine.

The rate of silylation decreases in the series of alcohols $CH_3OH > n\text{-}C_3H_7OH > n\text{-}C_6H_{13}OH$ in parallel with the decrease of their acidity[36,37]. The decrease of the rate of silylation in the series $RNH_2 > R_3CONH_2 > RCONHSi(CH_3)_3$ takes place in parallel with the decrease of the nucleophilicity of these compounds[35].

6. Steric Effects

In many cases the mechanism and rate of silylation are determined by the steric factors associated with the silylating agent or the compound being silylated. Thus, in the interaction of organic acids with silylamines, the change in reaction mechanism may be caused by the steric hindrance in the compound being silylated. In particular, the silylation of benzoic acid proceeds via the S_Ni–Si mechanism. When substituents are introduced into the *ortho*-position, the mechanism changes to S_N2–Si.[26]

Secondary amines with a branched chain in the α-position relative to the nitrogen atom are silylated with greater difficulty than primary amines, which is due to steric hindrance[38]. Bulky substituents in certain primary amines and aminoacids preclude the introduction of a second trimethylsilyl group at the nitrogen atom when the starting materials are treated with diethyltrimethylsilylamine in the presence of ammonium sulphate[39].

According to some investigators[36,37], the decrease of the rate of hydrolysis and alcoholysis of chlorotriorganosilanes in the series water > methanol > propanol > 1-hexanol > isopropyl alcohol is due to the steric hindrance in the compound being silylated.

A study of the rate of hydrolysis of various disilazanes showed that bulky substituents at the silicon atom retard the reaction[40]. The same causes are probably responsible for the resistance to hydrolysis of alkoxyisopropyldimethyl- and alkoxy-t-butyldimethyl-silanes[41,42]. A steric effect of the substituents at the nitrogen atom was also observed in a study of the rate of methanolysis of silylamines: $C_6H_5(C_2H_5).NSi(C_2H_5)_3$ silylates methanol more slowly than does $C_6H_5NHSi(C_2H_5)_3$.[14]

7. The Influence of Catalysts

The role of the acid catalyst in the silylation reactions proceeding via Eqns. (1) and (3) reduces to the protonation of the silylating agent R_3SiX, which in its turn weakens the $(p - d)_\pi$ interaction between the silicon atom and the group X. Examples of acid-catalysed silylation reactions are quoted below.

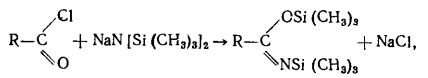
Alcoholysis of silylamines is as a rule an acid-catalysed reaction[14,26]. Grubb showed[13] that the condensation of a silanol in ethanol is catalysed by acids (see Subsection 1 of the present Section).

The following mechanism has been proposed for the silylation of alcohols and amines by hexamethyldisilazane[43]:

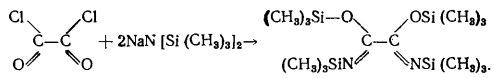
$$[(CH_3)_3Si]_2NH \overset{H^+}{\rightleftarrows} [(CH_3)_3Si]\overset{+}{N}H_2 - Si(CH_3)_3;$$

$$[(CH_3)_3Si]_3\overset{+}{N}H_2 + HY \rightleftarrows \{(CH_3)_3SiNH_2{-}Si(CH_3)_3\} \rightarrow (CH_3)_3SiY + (CH_3)_3Si\overset{+}{N}H_2,$$
$$\quad\quad\quad

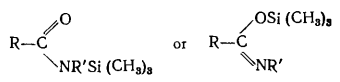
Another method for the synthesis of *NO*-bis(trimethylsilyl)amides was proposed by Pump and Rochow[65]:



where R = C_6H_5, C_5H_4N, or $(CH_3)_3C$. A trimethylsilyl derivative of oxalic acid diamide was obtained similarly[65]:

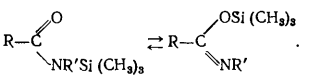


The structure of silylated amides. Silylation of amides can result in the formation of two isomeric products:



A B

^{1}H NMR data for a number of monotrimethylsilylated amides indicate the migration of the $(CH_3)_3Si$ group between oxygen and nitrogen atoms[15,66]:

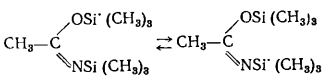


The equilibrium position in this process depends on the electronegativity of the substituents R and R′. The rate of migration of the $(CH_3)_3Si$ group varies in the following sequence of a function of R (R′ = C_6H_5):[66]

$$CF_3 \simeq CCl_3 < CHCl_2 < CH_2Cl < CH_3 \leqslant C_2H_5 < \text{iso-}C_3H_7 \ll \text{t-}C_4H_9 .$$

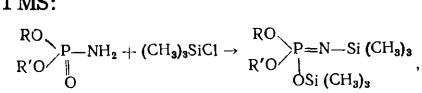
With increase of the electronegativity of the substituent at the nitrogen atom, the content of the *O*-trimethylsilyl imidate rises[15].

A study of the ^{1}H NMR and infrared spectra of bis(trimethylsilyl)acetamide (BSA) led Pump and Rochow[65] to the conclusion that this compound is *NO*-bis(trimethylsilyl)acetamide and that there is a rapid intramolecular exchange of $(CH_3)_3Si$ groups¶.



In recent years studies of the infrared and ^{1}H NMR spectra of mono- and bis-(trimethylsilyl)amides enriched in ^{15}N established rigorously that BSA and other bis(trimethylsilyl) derivatives having the general formula $[RCON][Si(CH_3)_3]_2$, where R = iso-C_3H_7, t-C_4H_9, or CF_3, exist exclusively in the imidate form, while bis(trimethyl)formamide and the monosilylacetamides CH_3CONR–$Si(CH_3)_3$ (R = H or alkyl) are true amides[67–69].

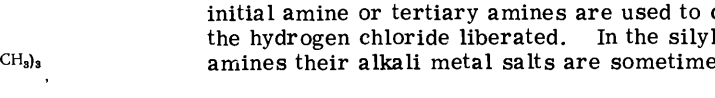
Dialkyl trimethylsilyl *N*-trimethylsilylphosphorimidates are formed on silylation of the corresponding amides of dialkyl phosphoric acids with an excess of CTMS:[70]



where R = R′ = CH_3; R = C_2H_5, R′ = CH_3; R = n-C_4H_9; R′ = CH_3. These compounds are very sensitive to moisture.

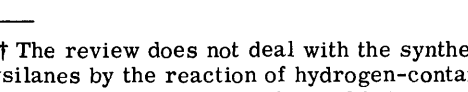
¶ We believe that the evidence supporting intramolecular rather than intermolecular exchange of $(CH_3)_3Si$ group is inadequate.

Vinyloxysilanes are formed when the corresponding enolates are acted upon by CTMS:[71]†



where R = H and R′ = C_6H_5, R = H and R′ = CH_3, R = CH_3 and R′ = $COCH_3$, or R = H and R′ = HC = $C(CH_3)_2$.

Lutsenko and coworkers[72] reported the synthesis of 2-trimethylsiloxyprop-1-ene by the exchange reaction between α-tripropylstannylacetone and CTMS:



Certain vinyloxysilanes have been obtained by treating α-mercurated aldehydes and ketones with chlorosilanes[73]. In addition we may note that, in the silylation of certain ketones with a BSA–*N*-trimethylsilylimidazole–CTMS mixture, trimethylvinyloxysilanes are also formed[74].

Silylating agents were already compared to some extent in the discussion of the mechanism of the silylation reaction. The most convenient are the trimethylsilyl derivatives of ureas and amides. To some extent, this can be accounted for by the fact that, as a result of the silylation reaction, ureas and amides, compounds which are usually inert with respect to silylation products, are formed. To investigate substances containing the NH,, OH, and SH groups with the aid of gas–liquid chromatography (GLC), they are silylated with trifluoro-*N*-methyl-*N*-trimethylsilylacetamide[57] and trifluoro-*NO*-bis(trimethylsilyl)acetamide[61], since the fluorinated derivatives are more volatile than their non-fluorinated analogues. Mixtures of several silylating agents have been recommended in several studies, CTMS being added to such compositions as the catalyst[7,75–77]. This version of the silylation reaction is used particularly frequently in GLC.

The employment of 2-trimethylsiloxyprop-1-ene for the silylation of compounds with the OH, NH, COOH, and SH groups showed that it is less effective than BSA and silylation with its aid is not always satisfactory[78]. *N*-Trimethylsilylimidazole, which readily silylates oxygen linked to mobile hydrogen, is at the same time relatively unsuitable for the silylation of the N–H bond[76].

The usefulness of a particular silylating agent is determined by the nature of the compound to be silylated. For this reason, examples illustrating conditions governing the silylation of various functional groups are quoted below.

IV. METHODS FOR THE SILYLATION OF VARIOUS CLASSES OF ORGANIC COMPOUNDS

1. Silylation of Amines

A general method for the silylation of amines involves their reaction with CTMS [2] (Table 1). An excess of the initial amine or tertiary amines are used to combine with the hydrogen chloride liberated. In the silylation of amines their alkali metal salts are sometimes used.

† The review does not deal with the synthesis of vinyloxysilanes by the reaction of hydrogen-containing silanes with αβ-unsaturated aldehydes and ketones.

Another method for the silylation of amines involves the transamination of silylamines, first investigated by Larson and coworkers[86]:

$$(CH_3)_3SiNR_2 + R'NH_2 \rightleftarrows (CH_3)_3SiNHR' + NHR_2.$$

Table 1. Silylation of amines by chlorotrimethylsilane.

Amine	Reaction product	Yield, %	Refs.
Ammonia	Hexamethyldisilazane	45-70	51,79
Methylamine	Methyltrimethylsilylamine	38-55	51
Ethylamine	Ethyltrimethylsilylamine	25	51
Diethylamine	Diethyltrimethylsilylamine	32	51
Aziridine	*N*-Trimethylsilylaziridine	44	80,81
Pyrrolidine	*N*-Trimethylsilylpyrrolidine	65	82
Piperidine	*N*-Trimethylsilylpiperidine	72	82
Pyrrole (K salt)	*N*-Trimethylsilylpyrrole	71	82,83
Indole (K salt)	*N*-Trimethylsilylindole	55	82
Aniline	*N*-Trimethylsilylaniline	60-80	84,85

Hexamethyldisilazane, trimethylsilylamine, and diethyltrimethylsilylamine are usually employed as donors of the trimethylsilyl group (Table 2). The rate of this reaction increases following the distillation of the amine NHR_2 formed or after the addition of catalytic amounts of ammonium salts, CTMS, or $ZnCl_2$, which promote the condensation to silazanes of the silylamines formed initially[38] (Table 3):

$$2\,(CH_3)_3SiNHR' \xrightarrow{(NH_4)_2SO_4} [(CH_3)_3Si]_2NR' + R'NH_2\ .$$

For sterically hindered amines, only the monosilyl derivatives have been obtained[38].

Table 2. Transamination of silylamines.

Amine	Silylating agent	Reaction product	Yield, %	Refs.
Imidazole	$[(CH_3)_3Si]_2NH$	*N*-Trimethylsilylimidazole	85	82
Pyrazole	$(C_2H_5)_3SiNH_2$	*N*-Trimethylsilylpyrazole	72	82
3,5-Dimethylpyrazole	$(C_2H_5)_3SiNH_2$	3,5-Dimethyl-*N*-trimethylsilylpyrazole	59	82
1,2,4-Triazole	$(C_2H_5)_3SiNH_2$	*N*-Trimethylsilyl-1,2,4-triazole*	81	82
Benzimidazole	$(C_2H_5)_3SiNH_2$	*N*-Trimethylsilylbenzimidazole	81	82
Indazole	$(C_2H_5)_3SiNH_2$	*N*-Trimethylsilylindazole	79	82
Pyrrolidine	$(C_2H_5)_3SiNH_2$	*N*-Trimethylsilylpyrrolidine	72	82
Piperidine	$(C_2H_5)_3SiNH_2$	*N*-Trimethylsilylpiperidine	42	82
Tetramethylenediamine	$[(CH_3)_3Si]_2NH$	*NN*-Bis(trimethylsilyl)tetramethylenediamine	89	87

*The position of the $(CH_3)_3Si$ group in the ring is not indicated.

The silylation of primary amines containing a branched alkyl substituent in the α-position with *N*-methyl-*N*-trimethylsilylacetamide yields monosilyl-substituted products[38]. In other cases silylation with this agent leads to the corresponding silazanes.

N-Methyl-*N*-trimethylsilylamides have been used to silylate secondary amines when the latter were analysed by GLC:[88]

$$RCON(CH_3)Si(CH_3)_3 + R'_2NH \rightarrow RCONHCH_3 + (CH_3)_3SiNR'_2,$$

where R = H or CH_3.

At an elevated temperature primary amines can be silylated by a trialkyl- or triarylsilane in the presence of catalytic amounts of metal hydrides[89]:

$$RNH_2 + R'_3SiH \xrightarrow[\sim 100^\circ]{\text{Met-H}} RNHSiR'_3 + H_2,$$

where R and R' is an alkyl or aryl group. Triarylsilanes react more readily in this process than trialkylsilanes. Likewise alkylamines are silylated less effectively than arylamines.

Table 3. Transamination of silylamines in the presence of catalysts[39].

Amine	Silylating agent	Catalyst	Reaction product	Yield, %
Ethylamine	$(CH_3)_3SiN(C_2H_5)_2$	$(NH_4)_2SO_4$	*N*-Ethylhexamethyldisilazane	85
n-Propyltrimethylsilylamine	ditto	ditto	Hexamethyl-*N*-(n-propyl)-disilazane	93
n-Butylamine	"	"	*N*-(n-butyl)hexamethyldisilazane	90
Aniline	"	"	Hexamethyl-*N*-phenyldisilazane	89
n-Butylamine	$[(CH_3)_3Si]_2NH$	"	*N*-(n-butyl)hexamethyldisilazane	33
Isopropylamine	$(CH_3)_3SiN(C_2H_5)_2$	"	Isopropyltrimethylsilylamine	95
n-Butylamine	ditto	$ZnCl_2$	n-Butyltrimethylsilylamine	90
t-Butylamine	"	$(NH_4)_2SO_4$	t-Butyltrimethylsilylamine	79
Cyclohexylamine	"	ditto	Cyclohexyltrimethylsilylamine	95

2. Silylation of Alcohols

Alcohols are usually silylated with the aid of CTMS (in the presence of tertiary amines) or hexamethyldisilazane. The reactions have comparatively low rates, but the desired products are formed in high yields. Best results were obtained when monosilylacetamides, BSA, and *N*-trimethylsilylimidazole were used. The rate of silylation of alcohols depend on their acidity and on steric factors (see Section II, Subsections 5 and 6).

Individual examples of the silylation of polyhydric alcohols and alcohols with other functional groups are quoted below. Prey and Gump[48], who silylated certain monosaccharides with CTMS in the presence of pyridine, obtained bis-, tris-, and tetrakis(trimethylsilyl)derivatives of monosaccharides. Schwartz et al.[52] reported the synthesis of incompletely silylated D-glucose with chlorotriethylsilane in pyridine. In the presence of a deficiency of the silylating agent the product is *O*-tris(triethylsilyl)-D-glucose, while in the presence of an excess of the silylating agent a mixture of tris- and tetrakis-(triethylsilyl)-D-glucoses is formed. Pentakis(trimethylsilyl)-glucose can also be obtained by silylating glucose with CTMS.[47]

Derivatives with all the hydroxy-groups trimethylsilylated were obtained by treating uronic acids with CTMS in the presence of pyridine[90]. Alcohols with sulphur-containing functional groups, for example $(C_3H_7S)_2C(CH_3).CH_2OH$, were silylated with CTMS in the presence of triethylamine[91]. Halogenophenols react with CTMS to form the corresponding trimethylsilyl derivatives[92]. Acetone cyanohydrin is also silylated with CTMS.[93,94]

Certain nitro- and halogeno-alcohols were recently silylated with the aid of halogenosilanes[19,95,96]:

$$(CH_3)_3SiCl + ROH \xrightarrow{C_5H_5N} (CH_3)_3SiOR,$$
$$R=CH_2CH_2NO_2,\ CH(CH_3)CH_2NO_2,\ CH_2NO_2,$$
$$CH(NO_2)C_2H_5,\ C(CH_3)_2CH_2NO_2,\ CH(CH_3)C(NO_2)(Br)CH_3,$$
$$CH_2C(Br)(NO_2)CH_3,\ CH(CH_2Cl)CH_2NO_2.$$

The silylation of sugars[97] and phenols[46,98] by hexamethyldisilazane gave high yields of the corresponding derivatives with all the hydroxy-groups trimethylsilylated. The silylation of alcohols, including steroid alcohols[77], by the BSA–CTMS–*N*-trimethylsilylimidazole mixture has been investigated at 60–80°C in several studies[74,77]. The resulting trimethylsilyl derivatives were analysed by GLC. It was found that this mixture of silylating agents is in some cases more effective than BSA.

The silylation of glucose and its derivatives by *N*-trimethylsilylacetamide has been reported[99]. The reactions proceed at high rates and with satisfactory yields. The silylation of polyhydric alcohols and sugars by *N*-methyl-*N*-trimethylsilylacetamide makes it possible to separate these compounds by GLC.[88] BSA readily silylates 2′-hydroxy-*m*-terphenyl, while 2,6-di-t-butylphenol reacts with BSA only on refluxing in acetonitrile[100]‡. The silylation of alcohols by trimethylvinyloxysilanes takes place with high yields in the presence of catalytic amounts of CTMS.[78]

3. Silylation of Aminoalcohols

Aminoalcohols are silylated by CTMS (in the presence of triethylamine)[101], hexamethyldisilazane[102], or dimethyltrimethylsilylamine[39]. These reactions have been mainly investigated for ethanolamine, the hydroxy-group being silylated first[101,102]:

$$HOCH_2CH_2NH_2 \xrightarrow[(C_2H_5)_3N]{(CH_3)_3SiCl} (CH_3)_3SiOCH_2CH_2NH_2$$

or

$$HOCH_2CH_2NH_2 \xrightarrow{[(CH_3)_3Si]_2NH} (CH_3)_3SiOCH_2CH_2NH_2.$$

Under more severe conditions and in the presence of an excess of the silylating agent, the *NO*-bis(trimethylsilyl) derivative of ethanolamine is produced[101]:

$$HOCH_2CH_2NH_2 \xrightarrow[(C_2H_5)_3N]{(CH_3)_3SiCl} (CH_3)_3SiOCH_2CH_2NHSi(CH_3)_3.$$

Ethanolamine has been silylated to *NN*-bis(trimethylsilyl)-*O*-trimethylsilylethanolamine with the aid of diethyltrimethylsilylamine in the presence of $(NH_4)_2SO_4$ as the catalyst[39].

It has been shown that the BSA–*N*-trimethylsilylimidazole mixture can silylate selectively the OH group in aminoalcohols in the presence CTMS.[74]

4. Silylation of Organic Acids

Trimethylsilyl esters of organic acids are usually obtained when the acids are treated with hexamethyldisilazane[98] or CTMS in the presence of pyridine[103]. For example, bis(trimethylsilyl) esters of terephthalic, fumaric, and sebacic acids have been obtained by treating the dibasic acids with CTMS.[103] Trimethyl acetate, propionate, and adipate have been synthesised with the aid of hexamethyldisilazane[98]. The silylation of derivatives of certain hydroxyacids has been studied[103].

When sodium tartrate is acted upon by CTMS, a mixture of products is formed: 2,3-bis(trimethylsilyl) derivatives of tartaric acid, polytartrate esters, trimethylsilanol, and hexamethyldisiloxane. The reaction of CTMS with strontium lactate results in the formation of polylactate esters, trimethylsilanol, and α-trimethylsiloxylactic acid, which the authors believe is obtained as a result of a rearrangement of monotrimethylsilyl lactate[103]:

$$\left[\begin{matrix}HOCHCOO\\ |\\ CH_3\end{matrix}\right]_2 Sr + 2(CH_3)_3SiCl \rightarrow SrCl_2 + 2\{CH_3CH(OH)COOSi(CH_3)_3\}$$
$$(CH_3)_3SiOCH(CH_3)COOH\ (65\text{—}70\%) + [-CH(CH_3)COO]_n + n(CH_3)_3SiOH.$$

In order to identify certain acids, their trimethylsilyl esters, which are suitable for infrared spectroscopic studies, are prepared with the aid of dialkyl trimethylsilyl *N*-trimethylsilylphosphorimidates[70]§:

$$RCOOH + (C_2H_5O)_2P[OSi(CH_3)_3]{=}NSi(CH_3)_3 \rightarrow (C_2H_5O)_2P(O)NHSi(CH_3)_3 + RCOOSi(CH_3)_3.$$

5. Silylation of Aminoacids

Aminoacids can be silylated by various agents: CTMS, hexamethyldisilazane, silylamines, and silylamides. In many cases best results were obtained when CTMS was used in the presence of triethylamine[104].

CTMS reacts with both the free acids and with their derivatives. The hydrogen of the carboxy-group is the first to be substituted in free aminoacids. It was found that monoaminoacids are converted into the corresponding hydrochlorides of their trimethylsilyl esters after only brief heating in the presence of an excess of CTMS.[105]:

$$H_2NCHRCOOH + (CH_3)_3SiCl \rightarrow HCl \cdot H_2NCHRCO_2Si(CH_3)_3,$$

where R = CH_3 or $CH_2CH(CH_3)_2$.

Aminoacids with several functional groups also form the hydrochlorides of *O*-trimethylsilyl esters on interaction with CTMS.[105] In particular, the hydrochlorides of the trimethylsilyl esters of glutamic acid, serine, and cystine have been obtained[105]. It is noteworthy that under these conditions lysine forms a mixture of mono- and tris(trimethylsilyl) derivatives[105]:

$$3H_2NCH_2(CH_2)_3CH(NH_2)COOH + 5(CH_3)_3SiCl \rightarrow 2\underset{\underset{NH_2\cdot HCl}{|}}{CH_2(CH_2)_3CHCO_2Si(CH_3)_3} + \underset{\underset{NH_2\cdot HCl}{|}}{}$$
$$+ \underset{\underset{NHSi(CH_3)_3}{|}}{CH_2(CH_2)_3CHCO_2Si(CH_3)_3}\ \underset{\underset{NHSi(CH_3)_3}{|}}{}.$$

The difficulty of silylating certain free aminoacids by chlorosilanes has been explained in a review[5] by the existence of inactive betaines. *O*-Trialkylsilyl esters of aminoacids sometimes disproportionate on heating[106]:

$$2RCH(NH_2)COOSiR'_3 \rightarrow RCH(NHSiR'_3)COOSiR'_3 + RCH(NH_2)COOH.$$

When the hydrochlorides of trimethylsilyl esters of aminoacids are treated with CTMS and triethylamine, *NO*-bis-(trimethylsilyl) derivatives of the aminoacids can be isolated in low yields[105].

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‡ CTMS and hexamethyldisilazane do not enter into this reaction[100].

§ The use of silylamides for this purpose is ruled out, because the reaction results in their conversion into carbonyl compounds[70].

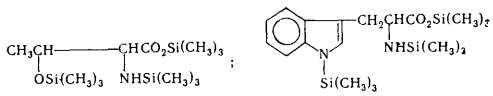
The silylation of aminoacids by hexamethyldisilazane leads to the formation of *NO*-bis(trimethylsilyl) derivatives and in this case too the hydrogen of the carboxy-group is the first to be substituted[106,107]§. A mixture of diethyltrimethylsilylamine, CTMS, and triethylamine is sometimes used to synthesis *NO*-bis(trimethylsilyl) derivatives of aminoacids[106].

Satisfactory results were obtained in the silylation of aminoacids by diethyltrimethylsilyl- or dibutyltrimethylsilyl-amines in the presence of catalytic amounts of $(NH_4)_2SO_4$. *NO*-Bis(trimethylsilyl) derivatives of valine, alanine, phenylalanine, leucine, and isoleucine were isolated in this way[39,108]. It was possible to introduce three $(CH_3)_3Si$ groups only into the sterically unhindered glycine molecule[39]:

$$H_2NCH_2COOH + 3(CH_3)_3SiN(C_2H_5)_2 \xrightarrow{(NH_4)_2SO_4} [(CH_3)_3Si]_2NCH_2CO_2Si(CH_3)_3 + 3NH(C_2H_5)_2.$$

A number of aminoacids with functional groups and their hydrochlorides have been silylated with the aid of diethyltrimethylsilylamine. In particular, derivatives of glutamic acid, sarcosine, alanine, histidine, proline, norvaline, tyrosine, hydroxyproline, and aspartic acid with all the functional groups trimethylsilylated have been obtained[109].

Klebe et al.[110] separated aminoacids by gas–liquid chromatography after silylating them with the aid of BSA. They investigated the silylation of more than 20 aminoacids, including alanine, valine, and serine. They were the first to describe the fully silylated threonine and tryptophan:



Trifluoro-*NO*-bis(trimethylsilyl)acetamide has also been proposed as a silylating agent for aminoacids[64]. Because of its volatility, it is more suitable for the gas–liquid chromatographic analysis of aminoacids than BSA.

The effects of silylating agents of different classes on certain aminoacids (phenylalanine, lysine, and tyrosine) were compared under the conditions of gas–liquid chromatography[76]. They were arranged in the following sequence in terms of the rate of silylation: dialkyltrimethylsilylamines > BSA ≫ monosilylacetamide. *N*-Trimethylsilylimidazole proved to be inactive under these conditions. It is interesting that the addition of dimethylformamide or dimethylformamide and CTMS to BSA impaired the silylating capacity of the latter, while pyridine facilitated silylation. Trifluorobis(trimethylsilyl)-acetamide was regarded as equal to BSA in its silylating capacity. The authors arranged in the following sequence the aminoacids investigated in terms of the rate of silylation: tyrosine ≥ phenylalanine > lysine. The above series do not involve the absolute kinetic characteristics of the process, since they reflect not only the rate of silylation but also the stability of the derivatives formed in solution.

It has been shown[75] that properties of the solvent have a significant influence on the degree of silylation of polyfunctional aminoacids. With increase of solvent polarity the degree of silylation of these products usually rises.

By treating alkyl esters of aminoacids with CTMS, Birkofer and Ritter[111,112] obtained their *N*-trimethylsilyl derivatives:

$$H_2NCHR(CH_2)_nCO_2C_2H_5 \xrightarrow{(CH_3)_3SiCl} (CH_3)_3SiNHCHR(CH_2)_nCO_2C_2H_5,$$

where $n = 0$ and R = H, n-C_3H_7, or s-C_4H_9 and $n = 1$ and R = H or CH_3.

N-Benzoyl derivatives of aminoacids react with CTMS to form *N*-benzoyl-substituted trimethylsilyl esters[113]:

$$C_6H_5CONHCHRCO_2H + (CH_3)_3SiCl \xrightarrow{C_5H_5N} C_6H_5CONHCHRCO_2Si(CH_3)_3,$$

where R = H, CH_3.

On silylation with CTMS in the presence of pyridine and formamide, glutamic acid gives rise only to the mono-*O*-trimethylsilyl derivatives, because (according to the authors) the amino-group and the second carboxy-group form an inner salt[113].

Ruhlmann[114] obtained trimethylsilyl-substituted aminoacids by treating alkali metal salts of the aminoacids with CTMS and triethylamine. He then isolated fully trimethylsilylated glycine, alanine, phenylalanine, and ϵ-aminocaproic, *p*-aminobenzoic, anthranilic, and glutamic acids. Treatment of glycine, alanine, and isoleucine hydrochlorides with CTMS and triethylamine led to the formation of the corresponding *NO*-bis(trimethylsilyl) derivatives of the aminoacids[115].

6. Silylation of Peptides

Like aminoacids, peptides have been silylated by treatment with CTMS,[111] hexamethyldisilazane[116], silylamines[117], and silylamides[104]. Both the carboxy- and amino-groups were silylated in the resulting products. When hexamethyldisilazane was used, only dioxopiperazines were isolated from the reaction mixture[116].

7. Silylation of Ketoximes and Aldoximes

These compounds are silylated by CTMS in pyridine[118-120]:

$$RR'C{=}NOH + (CH_3)_3SiCl \xrightarrow{C_5H_5N} RR'C{=}NOSi(CH_3)_3$$
$$R{=}R'{=}CH_3;\ R{=}R'{=}\text{iso-}C_5H_7;\ R{=}C_6H_5,\ R'{=}CH_3;$$
$$R{=}H,\ R'{=}CH_3;\ R{=}H,\ R'{=}C_6H_5;\ R{=}H,$$
$$R'{=}o\text{-}C_6H_4OH;\ R{=}H,\ R'{=}o\text{-}(CH_3)_3SiOC_6H_4.$$

8. Silylation of Hydroxylamine

When hydroxylamine is silylated by an equimolar amount of CTMS, *O*-trimethylsilylhydroxylamine is formed[121]. When the reaction is carried out in the presence of triethylamine and an excess of CTMS, the product is *NO*-bis(trimethylsilyl)hydroxylamine[121]:

$$NH_2OH + 2(CH_3)_3SiCl \xrightarrow{(C_2H_5)_3N} (CH_3)_3SiNHOSi(CH_3)_3.$$

The second hydrogen atom at the nitrogen atom can be substituted by the trimethylsilyl group only via the lithio-derivative[121]:

$$(CH_3)_3SiNH \xrightarrow[OSi(CH_3)_3]{C_4H_9Li} (CH_3)_3SiNOSi(CH_3)_3 \xrightarrow[Li]{(CH_3)_3SiCl} [(CH_3)_3Si]_2NOSi(CH_3)_3.$$

When CTMS was allowed to react with *O*- and *N*-alkyl derivatives of hydroxylamine, products with both one and two hydrogen atoms substituted by the $(CH_3)_3Si$ group were obtained[122].

¶*O*-Trimethylsilyl derivatives of aminoacids can be obtained by treating the *NO*-bis(trimethylsilyl) derivatives with ammonia of the free aminoacid[107].

9. Silylation of Hydrazines

When *O*- and *N*-alkyl derivatives of hydroxylamine are treated with CTMS, the product is 1,2-bis(trimethylsilyl)-hydrazine[123,124]. Under more severe conditions, a mixture of 1,2- and 1,1-bis(trimethylsilyl)hydrazines is isolated[124-126]. It has been suggested[124] that both isomers are formed as a result of the interaction of CTMS with intermediate monosilylated hydrazine. It has also been found that 1,2-bis(trimethylsilyl)hydrazine rearranges to 1,1-bis(trimethylsilyl)hydrazine in boiling benzene in the presence of N_2H_4.HCl or triethylamine.

1-Methyl-2-trimethylsilylhydrazine was obtained from methylhydrazine and CTMS.[127] Other trimethylsilyl derivatives of hydrazine were synthesised from this compound[126]:

$$CH_3NHNHSi(CH_3)_3 \xrightarrow[2.(CH_3)_3SiCl]{1.C_4H_9Li} CH_3N[Si(CH_3)_3]NHSi(CH_3)_3 + CH_3NHN[Si(CH_3)_3]_2.$$

On heating above 100°C in the presence of $N_2H_3(CH_3)$.HCl, the resulting mixture isomerises[127]:

$$(CH_3)_3SiN(CH_3)NHSi(CH_3)_3 \rightleftarrows CH_3NHN[Si(CH_3)_3]_2 .$$

10. Silylation of Acetylenes

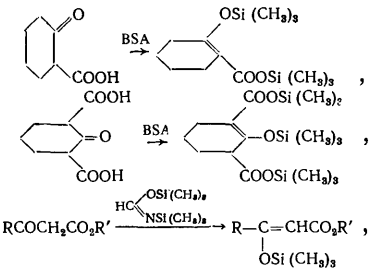
The silylation of free acetylenes has not been described, but there have been a number of studies dealing with the silylation of lithium, sodium, or magnesium derivatives of acetylenes by trialkylhalogenosilanes. Since it is comparatively difficult to remove the trialkylsilyl group from the acetylene silylation products, the term "silylation" is not used in the present sections strictly in the sense employed elsewhere in the review. However, since silylation is nowadays widely used to protect the terminal C≡C bond in order to use the resulting derivatives as intermediates in organic synthesis, we thought it desirable to include some information on this problem. The main data on the silylation of acetylenes up to 1960 have been compiled in a monograph[128]. Later a series of studies dealing with the silylation of metallated arylacetylenes (see for example, Eaborn et al.[129]), halogenoacetylenes[130], and unsubstituted acetylene (see, for example, Eastmond and Walton[131] and Krüerke[132]) were carried out.

11. Silylation of Ambident Systems

Bearing in mind the appreciable hardness of silyl cations[133], the interaction of silylating agents with ambident compounds may be expected to result in the silylation of the hardest anionic centre in these systems. However, in view of the relative lability of the silicon–element bonds, one can also postulate that both kinetically and thermodynamically favoured products of the silylation reaction should be detected in this case.

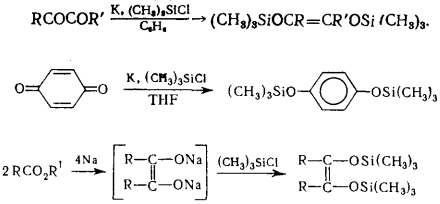
Silylation of ketones. As already mentioned, when carbonyl compounds are treated with a mixture of *N*-trimethylsilylimidazole with BSA and CTMS at an elevated temperature, the hardest centre in the ambident system—the oxygen atom—is silylated[74,77].

Silylation of α- and β-keto-acids and β-ketoacid esters. When these compounds were silylated by *NO*-bis(trimethylsilyl)amides, the corresponding *O*-trimethylsilyl derivatives were obtained[10,80]:

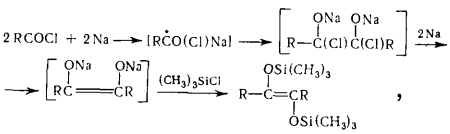


where R = CH_3, C_6H_5, or CH_3OCOCH_2 and R′ = CH_3 or C_2H_5.

Silylation of *O*- and *C*-metallo-derivatives of carbonyl compounds. The silylation of enolates usually leads to the formation of *O*-silylated products. When hydroxyketones[134], diketones[135], and carboxylic acid esters and chlorides[136-140] react with CTMS in the presence of alkali metals, it is suggested that the corresponding enolates are formed initially and then give rise to *O*-silylation products having the general formula $R'C[OSi(CH_3)_3]=CR[OSi(CH_3)_3]$, where R and R′ are alkyl substituents in the initial compounds. Several examples of this reaction are given below:

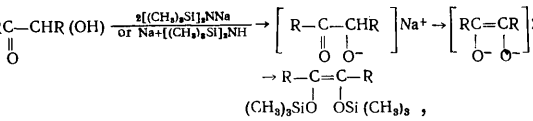


where R = CH_3, C_2H_5, C_3H_7, iso-C_3H_7, n-C_4H_9, $(CH_3)_2CH(CH_2)_2$, or n-C_7H_{15} and R′ = C_2H_5 or n-C_4H_9;



where R = H, CH_3, C_2H_5, or C_3H_7.

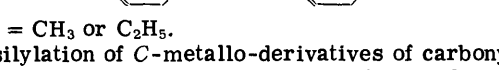
The sodium salt of hexamethyldisilazane may be used to synthesise *O*-metallo-derivatives of α-hydroxyketones[134]:



where R = H, CH_3, C_6H_5 or β-furyl and R′ = H, CH_3, C_6H_5, or β-furyl.

The interaction of carbonyl compounds capable of enolisation with the sodium salt of hexamethyldisilazane or of sodium enolates of carbonyl compounds with CTMS leads to the corresponding *O*-trimethylsilyl derivatives[71,141]. The reactions of alkyl- and alkylalkoxy-halogenosilanes with the sodio-derivatives of acetoacetic ester[142-144] or acetylacetone[145] leads to the formation of the corresponding *O*-silylated derivatives. The exchange reaction

of trialkylchlorosilanes with tributylstannoxycyclohex-1-ene provides a convenient method for synthesising trialkylsiloxycyclohex-1-enes[146,147]:



where R = CH_3 or C_2H_5.

The silylation of *C*-metallo-derivatives of carbonyl compounds also involves the formation of *O*-silylated products[148-151]. The reaction of *C*-metallo-derivatives of acetone with trialkylhalogenosilanes led to the formation of the corresponding alkoxysilanes[72,151]:

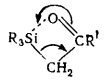
$$R_M CH_2COCH_3 \xrightarrow{R_3SiHal} CH_2=C(CH_3)OSiR_3 + R_MHal,$$

where R_M = $HgCH_2COCH_3$, HgCl, HgI, $(C_4H_9)_3Sn$, $(C_3H_7)_3Sn$, or $(C_3H_7)_3Ge$, R = CH_3, C_2H_5, or C_3H_7, and Hal = Cl, Br, or I.

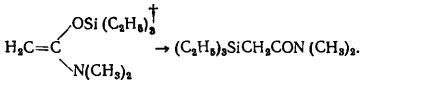
When trialkylhalogenosilanes were allowed to react with α-metallated carboxylic acid esters, only the *O*-silylation products were also isolated[72,151,152]:

$$(C_2H_5)_3SiI + Hg(CH_2COOCH_3)_2 \rightarrow CH_2=C(OCH_3)OSi(C_2H_5)_3 + HgCH_2COOCH_3;$$
$$(C_2H_5)_3SnCH_2COOCH_3 + (C_2H_7)_3SiI \rightarrow (C_2H_5)_3SnI + CH_2=C(OCH_3)OSi(C_3H_7)_3.$$

There is an equilibrium between the *O*- and *C*-silyl derivatives of carbonyl-containing compounds, which is usually displaced towards one of the products[150]. Isomerisation of silyl derivatives of carbonyl-containing systems can be an intramolecular[153-155] or an intermolecular[153,156] process. Since in the former case the optical configuration at the silicon atom is retained[155], it has been suggested that the reaction proceeds via a four-unit cyclic transition state:



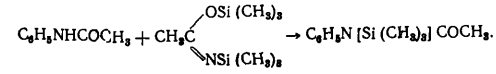
Intermolecular isomerisation is accelerated by trialkyliodosilanes or mercury salts[153-156]. The rate of isomerisation and the equilibrium position depend on the nature of the carbonyl compound and the substituents at the silicon atom. The introduction of electronegative substituents at the silicon atom facilitates the conversion into *C*-silylated products[157]. Substituents at the carbonyl group with a positive mesomeric effect also promote the rearrangement of *O*-derivatives into *C*-derivatives[158]:



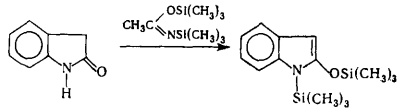
O-Silyl-derivatives are comparatively more favoured by thermodynamic factors, probably because of the $(p-d)\pi$ interaction between the oxygen and silicon atoms[150].

Silylation of amides, ureas, and urethanes. The silylation of amides has already been discussed. It was noted that the formation of these products is reasonable on thermodynamic grounds. Depending on the nature of the substituents at the carbonyl groups and at the nitrogen atom, the amide or imide form of the products predominates or their equilibrium mixture is formed.

In addition we may quote the study by Klebe et al.[100], who showed that amides can be silylated by BSA:



Under these conditions oxindole is immediately converted into the bis(trimethylsilyl) derivative[100]:



The silylation of phenyl esters of phosphoramidic acids with the aid of hexamethyldisilazane or methyltrimethylsilylamine yielded the corresponding trimethylsilyl derivatives[30,159]:

$$RN[Si(CH_3)_3]H + (NH_2)_nP(O)(OC_6H_5)_{3-n} \rightarrow [(CH_3)_3SiNH]_nP(O)(OC_6H_5)_{3-n},$$

where R = CH_3 or $Si(CH_3)_3$ and n = 1 or 2.

Some data on the silylation of ureas were presented above. Only the *N*-silylation products have been isolated. In addition to the foregoing, we may mention that urea can be silylated also by hexamethyldisilazane[88]:

$$CO(NH_2)_2 + [(CH_3)_3Si]_2NH \rightarrow [(CH_3)_3SiNH]_2CO + NH_3.$$

Mono-*N*-trimethylsilyl derivatives have also been obtained by treating the corresponding ureas with BSA.[100]

A number of studies have been made on the silylation of various urethanes by CTMS in the presence of triethylamine[160-162]:

$$RNHCOOR' \xrightarrow[(C_2H_5)_3N]{(CH_3)_3SiCl} RN[Si(CH_3)_3]COOR',$$

where R = alkyl[160,161] or C_6H_5 [162] and R' = CH_3, [160] $(CH_3)_3Si$, [161] or C_2H_5. [162] Kricheldorf[162] demonstrated rigorously by spectroscopic investigations that the products isolated are exclusively *N*-trimethylsilyl derivatives.

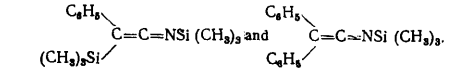
Silylation of compounds in which the mobile hydrogen atom has been replaced by a metal. When halogenosilanes react with silver cyanide[163-165], mixtures of silyl-substituted cyanides and isocyanosilanes, in equilibrium with one another, are formed. According to infrared spectroscopic data[166], the cyanide formed predominates the usual temperature, but with increase of temperature its content in the mixture falls.

The silylation of the corresponding silver salts by bis(trimethylsilyl) sulphide yielded $(CH_3)_3SiNC$ and $(CH_3)_3SiNCO$.[34] Trimethylsilyl nitrite is formed from silver nitrite and CTMS.[167]‡ The reaction of CTMS with silver cyanamide yields *NN*-bis(trimethylsilyl)carbodiimide, $(CH_3)_3SiN=C=NSi(CH_3)_3$, which is isomeric with cyanohexamethyldisilazane[169].

The tris(trimethylsilyl) derivative was obtained from the trisodium salt of acetonitrile and CTMS:[140]

$$Na_3[N\equiv C-C \leftrightarrow C=C=N] \xrightarrow{(CH_3)_3SiCl} [(CH_3)_3Si]_2C=C=N-Si(CH_3)_3.$$

The corresponding trimethylsilylated products were isolated similarly after the reaction of the sodium salts of phenylacetonitrile and diphenylacetonitrile with CTMS:[140]



Similar results were obtained by Klebe[170] in the silylation of malonotrile.

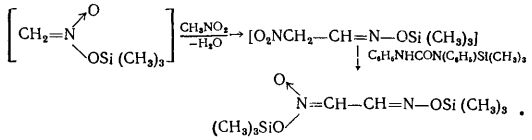
†H_2C = $CNR'_2(OSiR_3)$ is obtained by the interaction of $R_3SiNR'_2$ with keten[158].

‡ $(CH_3)_3SiONO_2$ was obtained similarly[168].

Silylation of diazoacetic ester. Schollkopf and coworkers[171,172] obtained diazo-*C*-trimethylsilylacetic ester by the interaction of diazoacetic ester salts with CTMS or bis(trimethylsilyl) sulphide:

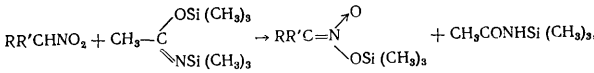
Silylation of nitro-compounds. Since nitro-compounds exhibit a dual reactivity[153], the formation of *O*-silylation products may be expected in their silylation reactions.

After allowing nitromethane to react with *NN'*-diphenyl-*N*-trimethylsilylurea, Klebe[170] isolated the bis(trimethylsilyl) derivatives of methazonic acid. The author suggests that this product is formed via the intermediate trimethylsilyl ester of methanenitronic acid:

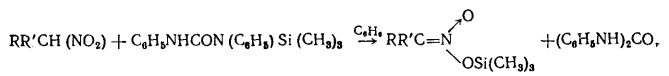


After the reaction of nitromethane with CTMS in pyridine, Manzur and Zamudio[174] isolated hexamethyldisiloxane, which they believe is also formed via the intermediate trimethylsilyl ester of methanenitronic acid. However, no evidence is adduced[170,174] in support of the formation of this intermediate.

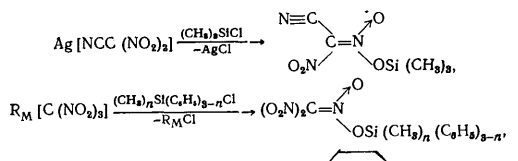
The first clear-cut experimental confirmation of the *O*-silylation of nitro-compounds was obtained by Tartakovskii and coworkers[155-159]. On silylation of nitroalkanes (nitromethane, nitroethane, etc.) by BSA, these investigators isolated (or detected) the trimethylsilyl esters of the corresponding alkanenitronic acids in nearly quantitative yields[175]:

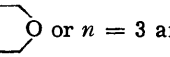


where R = R' = H (20°C)§, R = CH_3 and R' = H (60°C), R = C_2H_5 and R' = H (80°C), R = R' = CH_3 (100°C), or R = C_6H_5 and R' = H (20°C). *O*-Trialkylsilyl derivatives of aliphatic nitro-compounds with other functional groups have been obtained by treating the free nitro-compounds with *NN'*-diphenyl-*N*-trimethylsilylurea[176-179]:



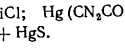
where R = R' = $COOCH_3$, R = $COOCH_3$ and R' = H, R = NO_2 and R' = H, or R = R' = NO_2, or by the interaction of the silver or mercury salts of the nitro-compounds with alkylchlorosilanes[176-179]:

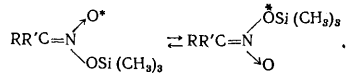


where n = 0, 1, or 3 and R_M = Ag.  or n = 3 and R_M = $Hg[C(NO_2)_3].CH_3NO_2$.

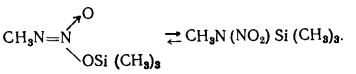
§ The silylation temperature is indicated in brackets.

The structure of the silyl esters of nitronic acids has been confirmed by making them undergo the 1,3-dipolar cycloaddition reaction with olefins and also by infrared, ultraviolet, and NMR spectroscopic data[176-180].

It has been shown[180] that there is a rapid intramolecular exchange of the $(CH_3)_3Si$ group between the oxygen atoms in the  fragment:



The silylation of methylnitramine by methyltrimethylsilylamine, BSA, or *NN'*-diphenyl-*N*-trimethylsilylurea as well as the silylation of the silver salt of methylnitramine by CTMS leads to a tautomeric mixture of *O*- and *N*-trimethylsilyl derivatives of methylnitramine[181]:



The presence of tautomers is indicated by low-temperature NMR data for the products[182]. It has been shown that, with increase of temperature, the equilibrium is displaced towards the *O*-trimethylsilyl derivative. The introduction of bulky substituents at the silicon atom has the same influence on the equilibrium position[182].

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The present review does not have as its aim the discussion of the problem of the applications of trimethylsilyl derivatives in organic synthesis. However, it is necessary to emphasise yet again that silylation makes it possible to expand significantly and modify the sphere of applications of particular products in organic reactions.

As examples, one can quote the interaction of silyldiamines with phosgene[87,183], the use of trimethylsilyl azide in the synthesis of tetrazoles[184,185], the thermal decomposition of silylated urethanes with formation of isocyanates[161], and the involvement of nitroalkane derivatives in dipolar 1,3-cycloaddition[178]. Furthermore, the uses of silyl derivatives in peptide synthesis[1,5] and in the synthesis of nucleosides and nucleotides[186] have been examined in detail.

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Indolizines

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The methods of synthesis and properties of indolizines—bicyclic condensed heterocylic compounds with a bridgehead nitrogen atom—are examined. The bibliography includes 201 references.

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I. INTRODUCTION

The studies on indolizines, which have been fairly vigorously prosecuted in recent years, are associated with the development of methods of synthesis and the investigation of this condensed system of pyridine and pyrrole with a bridgehead nitrogen atom as well as the search for physiologically active substances among indolizine derivatives.

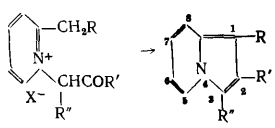
At the present time the chemistry of indolizines constitutes a fairly thoroughly investigated branch of the chemistry of heterocyclic compounds, which was founded by Scholtz and Chichibabin. Scholtz was the first to obtain 1,3-diacetylindolizine from α-picoline and acetic anhydride. He then converted it into indolizine (pyrrocoline).[1-4] Chichibabin elucidated the mechanism of this reaction[5,6]. He also developed one of the general and most convenient methods for the synthesis of indolizines from 2-methyl-*N*-β-oxoalkylpyridinium salts[7,8].

The chemistry of indolizines has been reviewed by Borrows and Holland[9] and a chapter in Mosby's monograph[10] is devoted to it. The present review surveys data on individual sections of indolizine chemistry and deals with recent studies which yielded new information both about the methods of synthesis and properties of indolizines.

II. SYNTHESIS OF INDOLIZINES

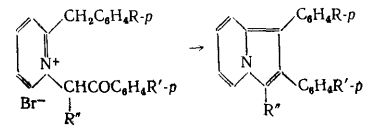
The Preparation of Indolizines from 2-Alkyl-*N*-(β-oxoalkyl)pyridinium Salts (The Chichibabin Method)

The closure of the five-membered ring of the indolizine system takes place on treating the salts formed from α-picoline (α-picoline substituted in the methyl group) and α-halogenoketones with sodium bicarbonate and certain other bases in aqueous, alcoholic, or acetone solutions:



Chichibabin obtained in this way 2-methyl, 2-phenyl, 2,5-dimethyl-, and 2-methyl-1-phenylindolizines[7,8].

This reaction was carried out both with and without isolation of the corresponding pyridinium salts. When α-bromoketones are used, substituted indolizines are formed in high yields—up to 90% for aryl-substituted derivatives[7,8,11-15]. A series of indolizines where the 2-position is occupied by a substituted phenyl or naphthyl group (with alkyl, halogeno-, nitro-, amino-, hydroxy-, alkoxy-, alkylthio-, phenylthio-, and other substituents)[16-26] as well as the *p*-arylphenyl[27], *p*-cyclohexylphenyl[28], 2-thienyl[29], 5-aryl-2-thienyl[30], *m*-(2,5-dimethylpyrrolyl)phenyl[31], 9-ethyl-3-carbazolyl[32], 2-dibenzofuryl[33], and 3-phenoxathiinyl[34] groups were obtained by this method, which was also used to synthesise 4,4-di-(2-indolizinyl)biphenyl from α-picoline and 4,4-di-(ω-bromoacetyl)biphenyl[35]. Indolizines with a methyl group in the 1-position were obtained from α-ethylpyridine[36,37]. α-Benzylpyridines with substituents in the benzene ring were used to synthesise 1,2-diaryl- and 1,2,3-triarylindolizines[38,39]:



In the synthesis of indolizines of this type quaternisation products were isolated[12,14]. It was not possible to isolate the quaternary salt formed from α-halogenoketones and 2-*p*-chlorobenzylpyridine, since it cyclises spontaneously to the corresponding substituted indolizine[38,40].

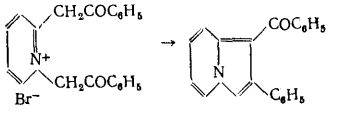
Only a limited number of studies have been made on the synthesis by this method of indolizines with substituents in the six-membered ring owing to the comparatively low availability of substituted α-picolines. 2,5-Dimethylindolizine was obtained by Chichibabin from αα′-lutidine and bromoacetone[7]. 2,6-Dimethyl-7-phenyl- and 6-methyl-2,7-diphenyl-indolizines[41], were obtained from 2,5-dimethyl-4-phenylpyridine[42]. 7-Benzyloxy-5-methyl-2-phenylindolizine was obtained in a very low yield from 4-benzyloxy-2,6-dimethyl-*N*-phenacylpyridinium bromide[43]. In the synthesis of 8-ethoxycarbonyl-2-methylindolizine (in 30% yield) ethyl 2-methylnicotinate and bromoacetone were used; the conversion of the resulting ester into 2-methylindolizine-8-carboxylic acid has been described[44].

Indolizines are formed from α′-substituted α-picolines in a lower yield than from α-picoline itself owing to steric hindrance due to the substituents at the $C_{(6)}$ atom of the pyridine ring[36]. A similar influence on the yield of indolizines was discovered for the sterically hindered

carbonyl group in halogenoketones[14,15,25]. The corresponding indolizine could not be synthesised from α-picoline and ω-bromo-4-(t-butyl)-2,6-dimethylacetophenone or ω-bromo-6-methoxy-2,4-dimethylacetophenone[25].

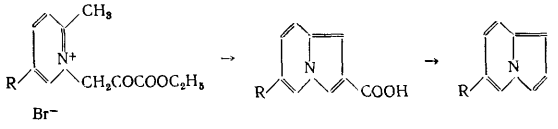
Vinylindolizines—2,3-dimethyl-6-vinyl- and 2-methyl-6-vinyl-derivatives—were obtained from 2-methyl-5-vinylpyridine and α-bromoethyl methyl ketone and bromoacetone respectively. The latter indolizine is resistant to polymerisation and oxidation in air[45,46]. 2-Methyl-5-vinylindolizine could not be isolated, because it polymerises during the reaction[47].

The synthesis of many indolizines with functional groups was achieved by the Chichibabin method. 1-Acetylindolizine could not be obtained from 2-acetonylpyridine and bromoacetophenone, because the corresponding quaternary salt is not formed[48]. However, 1,2-diphenacylpyridinium cyclises exclusively with formation of 1-benzoyl-2-phenylindolizine[49,50]:

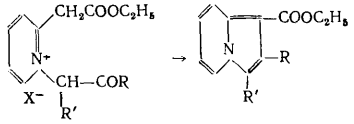


2-(*o*-Acetamidophenyl)-1-acetyl-indolizine was obtained in a yield of more than 40% by the cyclisation of 1-(*o*-acetamidophenacyl)-2-acetonyl-pyridinium salts[51]. 6-Ethoxycarbonyl(carbamoyl, cyano)-2-methyl- and 7-acetamidomethyl(cyano)-2-methyl-indolizines substituted in the six-membered ring were obtained by the cyclisation of 1-acetonyl-2-methylpyridinium bromides with the corresponding substituents in the pyridine ring[52].

Several versions of the synthesis of indolizinecarboxylic acids with carboxy-groups in the five-membered ring have been developed. The cyclisation of the quaternary salt formed from α-picoline and ethyl bromopyruvate gives a 30% yield of indolizine-2-carboxylic acid[14,53]. 6-Ethylindolizine-2-carboxylic acid was obtained in the same way from 5-ethyl-2-methylpyridine[54]. Indolizine[55,56] and 6-ethylindolizine were obtained by the decarboxylation of these acids[53]:



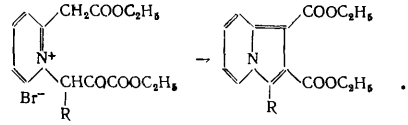
The cyclisation of the quaternary salts obtained from 2-ethoxycarbonylmethylpyridine and α-halogeno-substituted aldehydes and ketones leads to indolizine-1-carboxylic acids[57,58]. The above pyridine base and chloroacetone were used to synthesise 2-methylindolizine-1-carboxylic acid[59]. Salts obtained from the same pyridine base were used in the analogous condensation reaction with bromoacetaldehyde, α-bromopropionaldehyde, and bromophenylacetaldehyde. The corresponding indolizine-1-carboxylic acids are formed in comparatively low yields in the above reactions[49,57]:



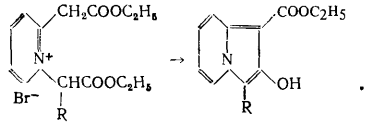
R=CH_3, R′=H; R=R′=H; R=H, R′=CH_3; R=H, R′=C_6H_5.

The synthesis of the methyl ester of 2-(*o*-acetamidophenyl)indolizine-1-carboxylic acid from 1-(*o*-acetamidophenacyl)-2-methoxycarbonylmethylpyridinium bromide has been described[60]. 1-Acetonyl-2-β-ethoxycarbonylethylpyridinium bromide and its analogue with a methoxy-group in the 4-position have been cyclised to 1-ethoxycarbonylmethyl-2-methyl- and 1-ethoxycarbonylmethyl-7-methoxy-2-methyl-indolizines. 1-(α-Ethoxycarbonylethyl)-2-methylindolizine was obtained from 2-(β-ethoxycarbonylpropyl)pyridine and bromoacetone in acetone, after which it was successively acetylated (benzoylated) at $C_{(3)}$ and then hydrolysed to 3-acetyl-(benzoyl)-1-(α-carboxyethyl)-2-methylindolizine[61]. The cyclisation of 2-(β-carbamoylethyl)-1-phenacylpyridinium bromide results in the formation of 1-carbamoylmethyl-2-phenylindolizine[43].

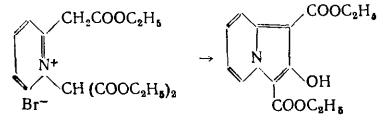
The diethyl ester of indolizine-1,2-dicarboxylic acid is formed in 95% yield in the Chichibabin cyclisation of the pyridinium salt obtained from 2-ethoxycarbonylmethylpyridine and bromopyruvic acid[49]. 2-Methoxycarbonylmethylpyridine was used in a similar condensation[58]. The esters of indolizine-1,2-dicarboxylic acids were also obtained with substituents in the 3-position[57]:



The reactions of quaternary salts formed from 2-ethoxycarbonylmethylpyridine and α-bromopropionate and bromophenylacetate esters are examples of syntheses of hydroxy-acids of the indolizine series. The ethyl esters of 2-hydroxy-3-methyl(phenyl)indolizine-1-carboxylic acids were obtained in this way[49].



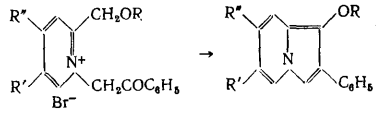
When the cyclisation is carried out in ether, the ethyl ester of 2-hydroxyindolizine-1-carboxylic acid is formed from 1,2-di(ethoxycarbonylmethyl)pyridinium bromide. When this reaction is carried out in the absence of a solvent, the ethyl esters of 3-ethoxycarbonylmethyl-2-hydroxyindolizine-1-carboxylic acid and 3-(1-ethoxycarbonyl-2-indolizinyl)-2-hydrozyindolizine-1-carboxylic acid are formed as a result of secondary reactions[49]. The diethyl ester of 2-hydroxyindolizine-1-carboxylic acid was obtained from 2-ethoxycarbonylmethylpyridine and bromomalonic ester[49]:



Indolizines with a cyano-group in the 1-position were obtained by the cyclisation of quaternary salts derived from 2-cyanomethylpyridine with α-bromoketones[49,62]. The ethyl ester of 3-cyano-2-methylindolizine-1-carboxylic acid was synthesised from 1-(α-cyanoacetonyl)-2-ethoxycarbonylmethylpyridinium bromide[63].

When 2-hydroxymethyl-1-phenacyl- or 2-acetoxymethyl-1-phenacyl-pyridinium bromide is treated with sodium bicarbonate, the product is 1-hydroxy-2-phenylindolizine—an unstable compound which rapidly darkens in air[63]. The cyclisation of 1-acetonyl(phenacyl)-2-ethoxymethyl-(phenoxymethyl)-5-methyl-4-phenylpyridinium bromide

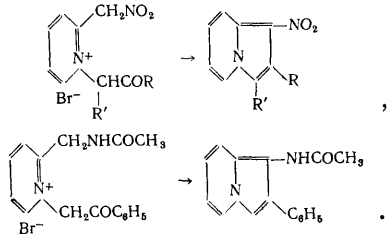
gave the corresponding substituted indolizines with an ethoxy- or phenoxy-group in the 1-position[41]:



R=R′=R″=H; R=C_2H_5, R′=CH_3, R″=C_6H_5; R′=CH_3, R=R″=C_6H_5.

An instance of the synthesis by the Chichibabin method of an indolizine with the hydroxymethyl group in the five-membered ring has been described. 1-Hydoxymethyl-2-methylindolizine was obtained in high yields by the cyclisation of 1-acetonyl-2-(β-hydroxyethyl)pyridinium bromide in sulpholan[52]. However, the cyclisation of 2-(β-hydroxypropyl)-1-phenacylpyridinium resulted in the formation of 2-phenylindolizine instead of the expected hydroxyalkylindolizine. It has been suggested that the hydroxyethyl group is split off during the reaction as a result of retro-aldol condensation[48].

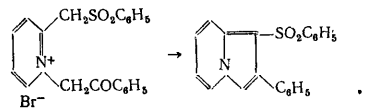
3-Nitroso-2-phenylindolizine is formed in the cyclisation of an α-picolinium salt with ω-chlorohydroxyimine-acetophenone[64]. The cyclisation of quaternary salts obtained from 2-nitromethylpyridine (hydrate) and bromoacetaldehyde, bromophenylacetaldehyde, bromoacetone, and bromoacetophenone results in the formation of 1-nitroindolizines in yields up to 50%.[63] 1-Acetamido-2-phenylindolizine was obtained in the same way from 2-acetamidomethyl-1-phenacylpyridinium bromide[63]:



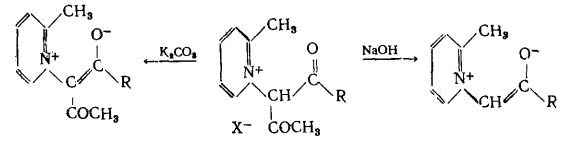
When 1-[2-(2-furyl)-1-isonitroso]-2-oxoethyl-2-picolinium chloride was treated with a 30% sodium hydroxide solution, 2-(2-furyl)-3-nitrosoindolizine was obtained in 87% yield[65].

A number of 1-aminomethyl-, 1-(β-aminoethyl)-, and 1-(γ-aminopropyl)-2-phenylindolizines with CH_3, $(CH_3)_2$, $COOC_2H_5$, and $CON(C_2H_5)_2$ substituents in the amino-group have been synthesised. The quaternary salts obtained from bromoacetophenone and the corresponding pyridines with ω-aminoalkyl-substituted amino-groups in the α-position were cyclised. Indolizines of this type with an alkylated amino-group were obtained by the reduction of an alkylcarbamoyl group with lithium tetrahydroaluminate after ring closure[50,66].

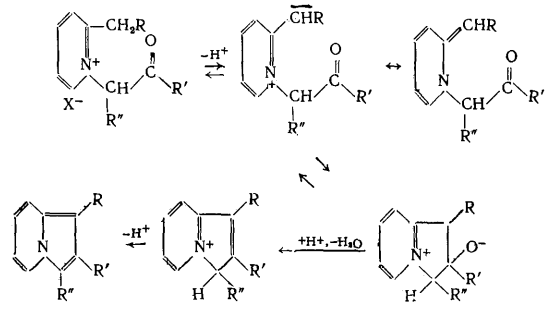
A sulphur-containing indolizine, phenyl 2-phenyl-1-indolizinyl sulphone, was synthesised from phenyl 2-picolinyl sulphone and bromoacetophenone[54,67]:



The mechanism of the formation of indolizines by the Chichibabin method has not as yet been fully elucidated. It has been discussed in detail by Bragg and Wibberley[49]. One of the initial factors serving as a basis for conclusions concerning the mechanism of this reaction was the difficulty encountered in the synthesis of certain indolizines by the Chichibabin method. It was not possible to cyclise salts obtained from α-picoline and α-chloroacetylacetone, α-bromobenzoylacetone, and ethyl α-bromobenzoylacetate[14,53]. Under the conditions of the cyclisation reaction, these salts, which are formed with difficulty, are converted into "enol-betaines". Then, depending on the nature of the salt and the base employed, either the acyl (ester) group splits off ("acid cleavage") or the enol-betaine is retained[68-72]:

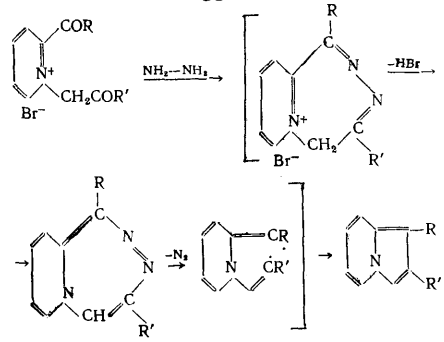


It has been suggested that fairly stable enol-betaines cannot cyclise and that indolizines are formed via a stage involving the condensation of the 1,3-ylid formed from the pyridinium salt when the latter is treated with a base[49]:



The formation of the ylid is facilitated when the substituent at the methyl group (at the carbon atom in the 2-position) has electron-accepting properties; it is also promoted by the use of sodium bicarbonate. The ylid cyclises intramolecularly via a reaction of the aldol type; the subsequent elimination of water from the betaine formed under these conditions followed by irreversible dehydrogenation of the 3*H*-indolizinium cation results in the formation of a substituted indolizine. Another hypothesis concerning the conversion of the ylid into a cyclic betaine has also been put forward: the methine obtained from the ylid cyclises[44].

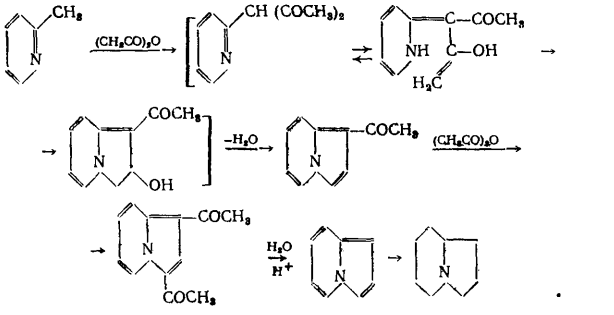
Hitherto the Chichibabin method has been one of the fundamental procedures for the synthesis of various indolizines. 1,2-Disubstituted indolizines, described by Kröhnke and Weis[73], were obtained by a different method from 2-acyl-1-(β-oxoalkyl)pyridinium salts. They were synthesised from 1-acetonyl(phenacyl)-2-acetyl(benzoyl)-pyridinium bromides and hydrazine hydrate. The following mechanism has been suggested for these reactions:



1,2-Disubstituted indolizines with a methyl or phenyl group in the 1-position and with a methyl or aryl group in the 2-position were synthesised by this method.

The Synthesis of Indolizines from α-Picoline (Substituted in the Methyl Group) and Acetic or Propionic Anhydride (the Scholtz Method)

The mechanism of the formation of 1,3-diacetylindolizine from α-picoline and acetic anhydride as well as the structure of the indolizine were elucidated by Chichibabin[1-7,74]:



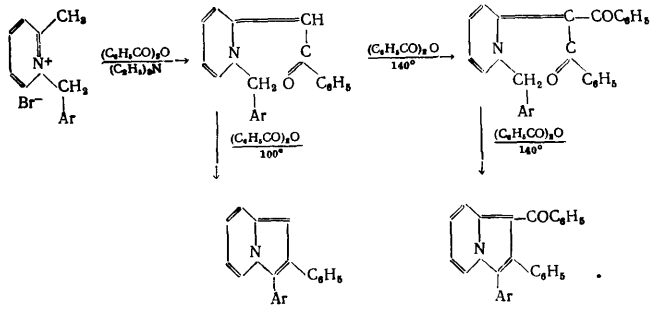
α-Picoline is acetylated to 2-diacetylmethylpyridine, the cyclisation of a tautomeric form of which gives rise to 1-acetyl-2-hydroxy-2,3-dihydroindolizine. Further dehydration leads to 1-acetylindolizine and the latter is acetylated to 1,3-diacetylindolizine. Deacetylation takes place on acid hydrolysis. Indolizine has been converted by catalytic hydrogenation into octahydroindolizine—δ-coniceine[55].

1,3-Diacetyl-5-methyl- and 1,3-diacetyl-5-phenylindolizines were obtained by the Scholtz method from the corresponding substituted α-picolines[3,75]. Only propionic anhydride as well as acetic anhydride can be used in this reaction[4,76]. The structure of the resulting 3-methyl-1-propionylindolizine was demonstrated by acetylating it to 3-methylindolizine[11].

The synthesis of 3-acetyl-1-(*p*-chlorophenyl)indolizine from 2-(*p*-chlorophenyl)methylpyridine by this method has been described[77]. 1-Acetyl-3-ethoxyindolizine were obtained by heating ethoxymethyl α-picolinyl ketone with acetic anhydride[78].

The Synthesis of Indolizines from 2-Alkyl-1-Benzylpyridinium Salts

When 1-benzyl-2-methylpyridinium salts are treated with acetic, propionic, or benzoic anhydrides in the presence of bases (for example triethylamine), the five-membered ring is closed at the $C_{(2)}-C_{(3)}$ bond, resulting in the formation of substituted indolizines. When the reaction is carried out at 100°C, 2,3-disubstituted indolizines are formed and at 140°C also 1,2,3-trisubstituted indolizines:



The pyridinium salt is benzoylated at the α-methyl group with simultaneous elimination of hydrogen bromide. This results in the formation of 2-benzoylmethylene-1-benzyl-1,2-dihydropyridine substituted in the benzene ring of the benzyl group. Its cyclisation at 100°C, which is an intramolecular aldol condensation, leads to the formation of 3-aryl-2-phenylindolizine. When the reaction is performed at 140°C, the methine derivative is benzoylated to 2-dibenzoylmethylene-1-benzyl-1,2-dihydropyridine, the cyclisation of which leads to 3-aryl-1-benzoyl-2-phenylindolizine. Since direct benzoylation of 3-aryl-2-phenylindolizine can be achieved only at 200°C, it is believed that a dibenzoylmethine derivative is formed as an intermediate in the above reactions[50,63,67,79,80]. In many cases monosubstituted methine derivatives were isolated and their conversion into indolizines was investigated. Methines are obtained on simultaneous acylation and dehydrohalogenation of 1-benzyl-2-methylpyridinium bromides[72,81,82].

1-Benzyl-2-phenacylidene-1,2-dihydropyridine was prepared in two ways: by the Schotten-Baumann benzoylation of 1-benzyl-α-picolinium bromide[81,83,84] and by the quaternisation of 2-phenacylpyridine[50,81]. On treatment with acetic anhydride in the presence of triethylamine, 2-benzoylmethylene- and 2-acetylmethylene-1-benzyl-1,2-dihydropyridine are converted in yields up to 90% into 1-acetyl-2,3-diphenyl- and 1-acetyl-2-methyl-3-phenylindolizines respectively[50,67]. Triethylamine can be successfully replaced in this reaction by sodium acetate[85]. When propionic anhydride was used in the first instance, the analogous indolizine with the propionyl group in the 1-position was obtained.

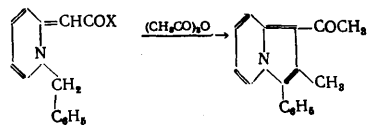
Methine derivatives are cyclised on being heated in formamide[79]. 6-Methyl-2,3,7-triphenylindolizine was obtained in this way from 1-benzyl-5-methyl-2-phenacylidene-4-phenyl-1,2-dihydropyridine; its cyclisation in the presence of acetic anhydride leads to its 1-acetyl-substituted analogue[82].

The corresponding indolizines with *p*-nitro- and *p*-chloro-phenyl groups in the 3-position were obtained, without the isolation of the methine derivatives, from 2-methyl-1-[*p*-nitro(*p*-chloro)]benzylpyridinium bromides and acetic or benzoic anhydride at 140°C with and without the acyl group in the 1-position in each case[79,80]. The influence on the yield of indolizines of the nature of the substituent in the *p*-position of the *N*-benzyl group which affects the reactivity of the *N*-methylene group was investigated. The following sequence of substituents in terms of increasing yields of indolizine caused by their introduction has been established: $p\text{-}NO_2C_6H_4 < C_6H_5 < p\text{-}CH_3OC_6H_4$.

1-Acetyl-2,3-dimethylindolizine was obtained in 9% yield from 1-ethyl-2-phenacylidene-1,2-dihydropyridine after heating for 12 h with acetic anhydride. The corresponding indolizine could not be obtained from 1-methyl-2-phenacylidene-1,2-dihydropyridine and benzoic anhydride. The product isolated in this case was 2-dibenzoylmethylene-1-methyl-1,2-dihydropyridine, which was also obtained by the direct benzoylation of 1-methyl-2-phenacylidene-1,2-dihydropyridine[80].

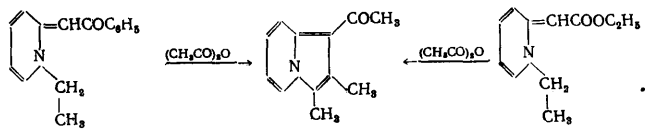
1,2,3-Triphenylindolizine[38] was synthesised by this method from 1,2-dibenzylpyridinium bromide and benzoic anhydride, while the use of acetic anhydride led to the isolation of 2-methyl-1,3-diphenylindolizine[79].

1-Acetyl-2-methyl-3-phenylindolizine is formed from 1-benzyl-2-cyanocarbonyl(carbamoyl, phenylcarbamoyl, acylcarbonyl)methylene-1,2-dihydropyridines and acetic anhydride[50]:

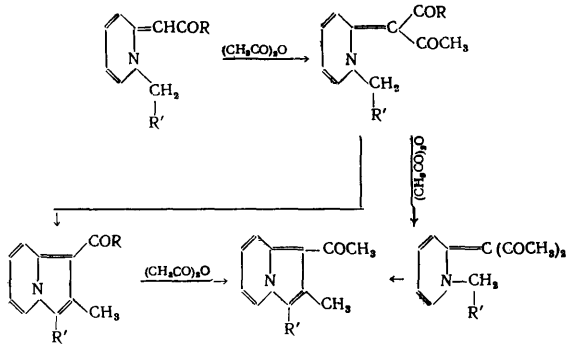


X=CN, NH_2, NHC_6H_5, COR.

1-Acetyl-2,3-dimethylindolizine was obtained similarly from 2-benzoyl(ethoxycarbonyl)methylene-1-ethyl-1,2-dihydropyridine:



It is believed that the first reaction stage is *C*-acetylation of the ketoenamine to a diacylmethine, which can then be converted into indolizine in two ways:



Initially the diacyl derivative undergoes transacylation and then cyclises. The second pathway involves the cyclisation of the diacylmethine derivative via the acetyl group followed by transacetylation at the 1-position. This is less likely because 1-ethoxycarbonyl- and 1-cyano-indolizines are stable in relation to acetic anhydride and ethoxycarbonyl and cyano-groups are not replaced by the acetyl group in these substances[50].

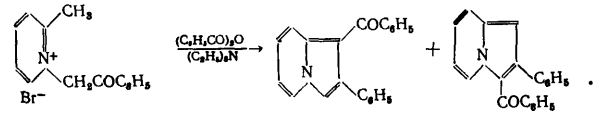
The occurrence of transacylation in the formation of indolizines from diacylmethines is confirmed to some extent by the following results obtained in the synthesis of indolizines from 1-benzyl-2-ethoxycarbonylmethylene-1,2-dihydropyridine[50,86]. When this methine was treated with acetic anhydride, 2-acetoxy-1-acetyl-3-phenylindolizine, 1-acetyl-2-methyl-3-phenylindolizine, and 1-ethoxycarbonyl-2-methyl-3-phenylindolizine were obtained in proportions of approximately 14 : 8 : 1. When this reaction was carried out in acetic acid, the ratios of the indolizines changed sharply and became 4 : 20 : 1. Thus the ethoxycarbonyl group is split off during the reaction (transacylation), which is promoted by an increase of the acidity of the medium[86].

Two methods have been described for the cyclisation of 1-(*p*-nitrobenzyl)-α-picolinium chloride to 3-(*p*-nitrophenyl)indolizine. This indolizine is formed in a low yield on heating the above picolinium salt with *s*-triazine in a pyridine–piperidine mixture; it is suggested that the intermediate in this reaction is 2-(β-aminovinyl)-1-(*p*-nitrobenzyl)pyridinium chloride. The second method involves heating the same picolinium salt in a pyridine–piperidine mixture with triethyl orthoformate: it is suggested that in this case the intermediate is 1-[β-ethoxy-α-(*p*-nitrophenyl)vinyl]-2-methylpyridinium chloride. 3-(*p*-Nitrophenyl)indolizine was obtained by the second method in 67% yield[87].

Synthesis of Indolizines from 2-Alkyl-1-(β-oxoalkyl)-pyridinium Salts and Acid Anhydrides

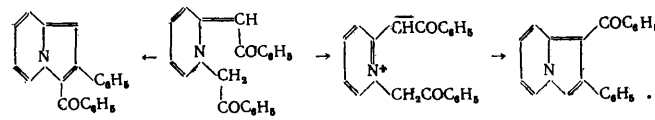
This method, as it were, combines two procedures for the synthesis of indolizines: their preparation by treating 2-alkyl-1-(β-oxoalkyl)pyridinium salts with bases and by treating 2-alkyl-1-benzylpyridinium salts with acid anhydrides, also in the presence of bases.

In one of these methods a 1-(β-oxoalkyl)pyridinium salt is treated with acetic anhydride in the presence of triethylamine. A mixture of 1-benzoyl-2-phenylindolizine and 3-benzoyl-2-phenylindolizine was obtained in this way in a satisfactory yield in proportions of 1 : 2 from 2-methyl-1-phenacylpyridinium bromide, benzoic anhydride, and triethylamine at 140°C.[44,79,80] The same indolizines were obtained in the same proportions when the initial pyridinium salt was treated with benzoic anhydride in the presence of sodium benzoate[44]:

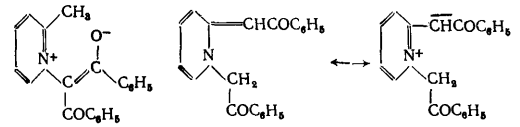


3-Acetyl-2-methylindolizine (58%) and 1,3-diacetyl-2-methylindolizine (27%) were obtained from 1-acetonyl-2-methylpyridinium bromide, acetic anhydride, and sodium acetate[44]. The synthesis of analogues of the same indolizines with substituents in the six-membered ring was achieved by the same procedure.

1-Ethoxycarbonyl-3-methylindolizine was obtained in 47% yield on heating 2-ethoxycarbonylmethylpyridine with α-bromopropionaldehyde in acetic anhydride[88]. The following syntheses of 1-benzoyl-2-phenyl- and 3-benzoyl-2-phenyl-indolizines, mentioned above, and also 2-phenylindolizine apparently constitute important evidence which can be used for the solution of problems concerning the mechanisms of the formation of indolizines from 2-alkyl-1-(β-oxoalkyl)pyridinium salts and acid anhydrides. The first two indolizines were formed (in proportions of 1 : 5) when 1-phenacyl-2-phenacylidene-1,2-dihydropyridine was treated with acetic anhydride. It was suggested that 3-benzoyl-2-phenylindolizine is formed directly from the methine derivative (ring closure at the 2–3 positions) and 1-benzoyl-2-phenylindolizine is formed from the intermediate ylid (ring closure at the 1–2 positions[49,50]:

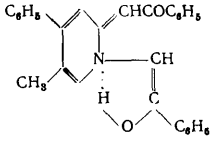


Different structures have been attributed to the product formed on benzoylation of 2-methyl-1-phenacylpyridinium bromide: enol-betaine[71,80] as well as 1-phenacyl-2-phenacylidene-1,2-dihydropyridine and its mesoform as the betaine-anion (ylid)[50]:



The enol-betaine was synthesised from α-picoline and dibenzoylmethyl bromide. It was established that hydrobromic acid cleaves it to benzoic acid and 2-methyl-1-phenacylpyridinium bromide.

An enolic structure with an intromolecular hydrogen bond was attributed to 5-methyl-1-phenacyl-2-phenacylidene-4-phenyl-1,2-dihydropyridine on the basis of its spectroscopic characteristics:

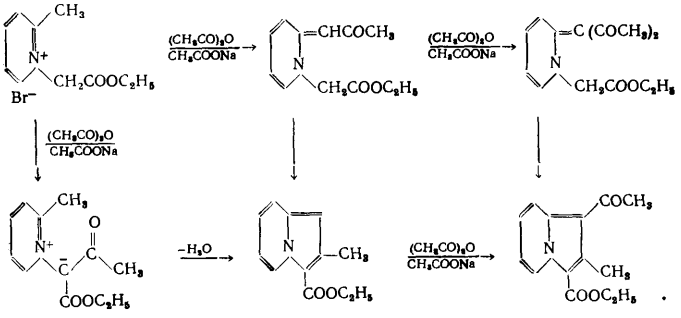


When this methine derivative was heated with acetic anhydride, 3-benzoyl-6-methyl-2,7-diphenyl-, 1-benzoyl-6-methyl-2,7-diphenyl-, and 1-acetyl-3-benzoyl-6-methyl-2,7-diphenyl-indolizines were obtained. The second indolizine is formed on cyclisation of the methine derivative in the presence of formamide[89]. 3-Benzoyl-2-phenyl- and 1-benzoyl-2-phenyl-indolizines were synthesised from the stable 2-methylpyridinium dibenzoylmethylid on brief heating with acetic anhydride[79,80].

Analysis of the type of substitution in the indolizines formed on treatment of 2-alkyl-1-(β-oxoalkyl)pyridinium salts with acid anhydrides in the presence of triethylamine or the sodium salt of the acid led Dainis[44] to the hypothesis that the first reaction stage involves the conversion of the pyridinium salt into ylids. The Table[44] illustrates examples of this reaction.

The method of synthesis of indolizines from 2-alkyl-1-(β-oxoalkyl)pyridinium salts with the aid of acetic anhydride and sodium acetate (as well as propionic anhydride and sodium propionate) has been used in the synthesis of indolizinecarboxylic acids. A mixture of the ethyl ester of 2-methylindolizine-3-carboxylic acid (the main product) and the ethyl ester of 1-acetyl-2-methylindolizine-3-carboxylic acid was obtained by this method in a good yield from 1-ethoxycarbonylmethyl-2-methylpyridinium bromide (3-cyanosubstituted analogues of these indolizines were also obtained from 1-cyanomethyl-2-methylpyridinium). The ethoxycarbonyl group in these indolizines is readily removed on acid hydrolysis[85].

The following explanation has been proposed for the formation of substituted indolizines by this method, which is illustrated by the syntheses of the above indolizines.

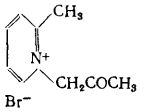
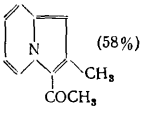
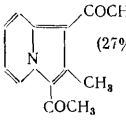
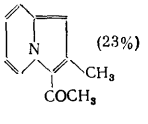
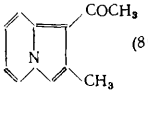
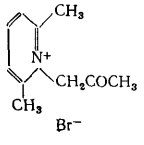
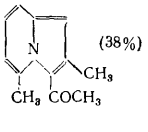
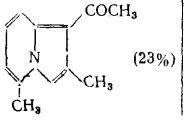
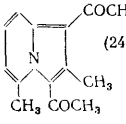
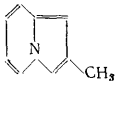


Bearing in mind that 3-ethoxycarbonyl-2-methylindolizine greatly predominates in the mixture of indolizines obtained and that direct acetylation of this indolizine with acetic anhydride in the presence of sodium acetate gives rise to 1-acetyl-3-ethoxycarbonyl-2-methylindolizine in a low yield (12%, the remainder consists of the initial indolizine), it is suggested that kinetically the rate-limiting stage is the formation of the diacylmethine[85]. Quantitative data for the synthesis of indolizines from 1-methoxycarbonylmethyldimethylpyridinium salts are consistent with this conclusion. When the methyl groups in the pyridine ring are in the 2,4- and 2,5-positions, a mixture of indolizines non-acylated and acylated at $C_{(1)}$ is formed; on the other hand, when the methyl groups are in the 2,3-positions, only 3-acetyl-2,8-dimethylindolizine is produced (70% yield). The explanation is that the methyl group at $C_{(3)}$ in the pyridine ring causes steric hindrance to the acylation of the intermediate acylmethine to the diacylmethine.

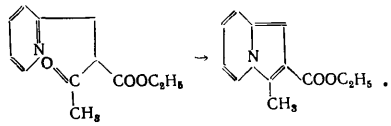
Cyclisation of 2-(γ-oxoalkyl)pyridines

The initial substituted pyridines of this type are obtained from 2-bromomethylpyridine and sodio-derivatives of acetoacetic and malonic esters as well as acetylactone[90]. The cyclisation is achieved by heating 2-(γ-oxoalkyl)pyridine with acetic anhydride for a short time[63].

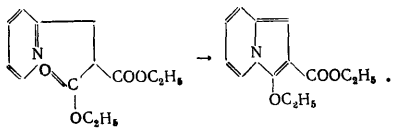
Indolizines obtained from 1-acetonyl-2-methyl(2,6-dimethyl)pyridinium bromides.

Starting compound	Method	Indolizines isolated			
	$(CH_3CO)_2O$ + CH_3COONa	 (58%)	—	 (27%)	—
	$(CH_3CO)_2O$ + $(C_2H_5)_3N$	 (23%)	 (8%)	—	—
	$(CH_3CO)_2O$ + CH_3COONa	 (38%)	 (23%)	 (24%)	

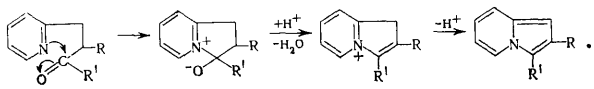
The condensation of 2-($\beta\beta$-diacetylethyl)pyridine leads to the formation of 2-acetyl-3-methylindolizine. The more active carbonyl group enters into cyclisations of this type, which has been shown in the conversion of 2-(β-acetyl-β-ethoxycarbonylethyl)pyridine into the ethyl ester of 3-methylindolizine-2-carboxylic acid:



As expected, bearing in mind the foregoing considerations, the cyclisation of 2-[$\beta\beta$-di(ethoxycarbonyl)ethyl]-pyridine to the ethyl ester of 3-ethoxyindolizine-2-carboxylic acid proceeds with greater difficulty and with a lower yield under comparable conditions:



It is believed that the cyclisation reaction begins with nucleophilic attack by the nitrogen atom on the carbonyl group in the side chain, which leads to ring closure with formation of a betaine. The protonation of the latter and subsequent dehydration result in the formation of an indolizinium cation, which is converted into a substituted indolizine by acid-catalysed dehydrogenation:

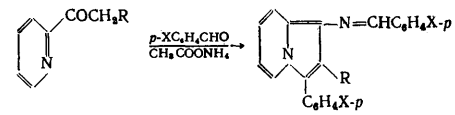


An indolizine is probably formed similarly (in 50% yields) from 3-(2-pyridyl)-1-propanol when it is heated in the presence of palladium on charcoal, since the intermediate should be 3-(2-pyridyl)propanol. 5-Methyl-2-phenylindolizine was obtained by the same procedure from 3-(6-methyl-2-pyridyl)-2-phenylpropanol[75]. It is suggested that 3-(2-pyridyl)indolizine is formed in the same way from 1,1-diacetoxy-1,3-di-(2-pyridyl)propane when it is heated *in vacuo*[91]. Pyrolysis of 2-($\alpha\gamma$-diacetoxypropyl)pyridine leads to the formation of indolizine[92]. 5-Methylindolizine was obtained similarly in a low yield by the pyrolysis of 2-($\beta\gamma$-diacetoxypropyl)-6-methylpyridine. The same indolizine was formed in 30% yield on pyrolysis (at 450°C) of 2-(α-acetoxypropenyl)-6-methylpyridine[75].

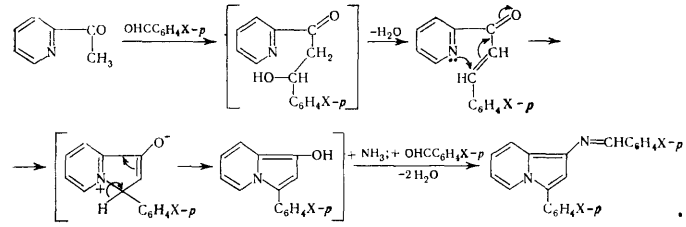
When 2-(γ-hydroxypropyl)pyridine *N*-oxide is treated with acetic anhydride, the product is 2-(γ-acetoxy-α-acetylpropyl)pyridine, which cyclises to an indolizine at 480°C with elimination of two acetic acid molecules[92]. On treatment with concentrated sodium hydroxide, 2-(γ-chloro-β-hydroxypropyl)pyridine, formed in a low yield on partial reduction of 2-(γ-trichloro-β-hydroxypropyl)pyridine with zinc in dilute sulphuric acid, is converted into an indolizine in a low yield[93]. The reaction of 2-pyridyl-lithium with epichlorohydrin leads to 2-hydroxy-3*H*-indolizinium chloride from which an indolizine was obtained on treatment with sodium hydroxide[94].

The Cyclisation of 2-Cinnamoylpyridines

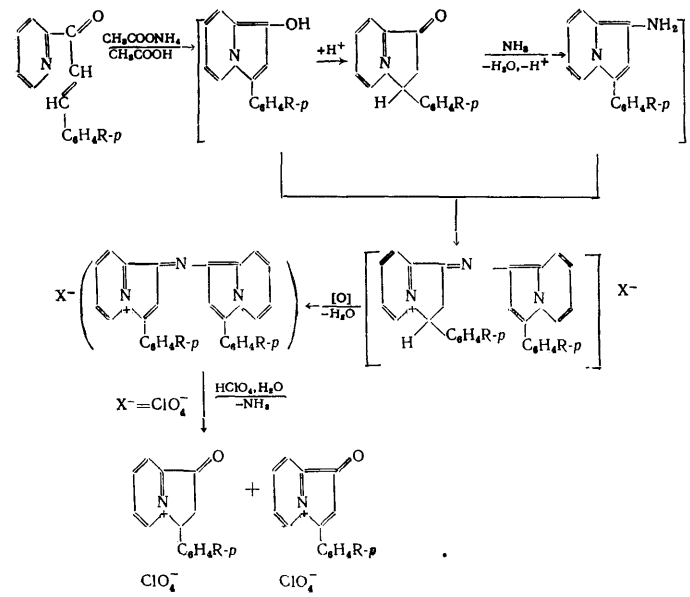
When 2-acetyl(propionyl, benzoyl)pyridines are heated with aromatic aldehydes in glacial acetic acid in the presence of ammonium acetate (with an acylpyridine : aldehyde ratio of 1 : 2), azomethines derived from 1-aminoindolizines are formed in yields up to 50%:[95-97]



The first stage of this reaction is the aldol condensation of 2-acylpyridine with the aromatic aldehyde, which results in the formation of 2-cinnamoylpyridine. Its intramolecular condensation leads to the formation of 3-aryl-1-hydroxyindolizine. On interaction of the latter with ammonia, the hydroxy-group is replaced by the amino-group and 1-amino-3-arylindolizine then condenses with the aromatic aldehyde[97-101]:



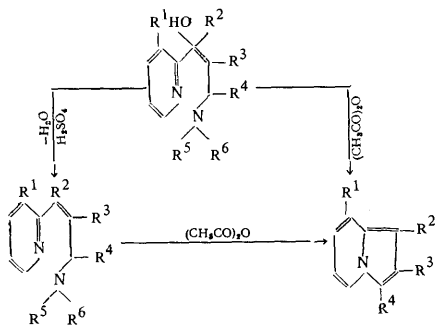
When 2-cinnamoylpyridines and ammonium acetate are heated in glacial acetic acid in the presence of air, the products are also azocyanines, but this time with two indolizine rings, which can be isolated in the form of salts. It is suggested that 3-aryl-1-hydroxyindolizine, whose salt has the 3-aryl-1-oxo-2,3-dihydro-1*H*-indolizinium structure, and 1-amino-3-arylindolizine formed from it condense. The intermediate dihydroazomethine is then oxidised further by atmospheric oxygen to the azomethine:



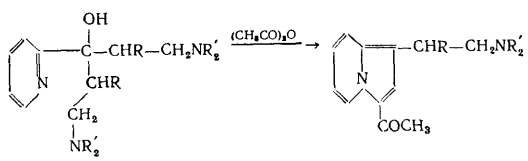
When the perchlorate of such an azomethine ($X^- = ClO_4^-$) is heated with 70% perchloric acid, it is cleaved with formation of 3-aryl-1-oxo-2,3-dihydro-1*H*-indolizinium and 3-aryl-1-oxo-1*H*-indolizinium perchlorates[102].

Deamination and Cyclisation of 2-(γ-dialkylamino-α-hydroxyalkyl)pyridines

On heating with acetic anhydride, the aminoalcohols formed from 2-lithiopyridines and β-dialkylaminoketones[103] are converted into substituted indolizines in yields up to 60%. The same indolizines are formed under the same conditions from the dehydration products of 2-(γ-dialkylamino-α-hydroxyalkyl)pyridines. When R^4 = H (see the reaction scheme), indolizines acetylated in the 3-position are obtained[77,104-106]:

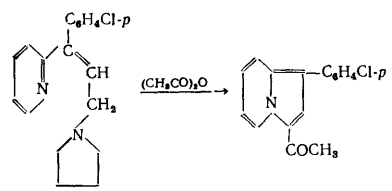


3-Acetyl-1-(*p*-chlorophenyl)indolizine together with a number of side products were obtained in this way from 1-(*p*-chlorophenyl)-1-(2-pyridyl)-3-(1-pyrrolidinyl)-1-propanol. The use of diaminomethanols (symmetric and asymmetric) in these reactions permitted the synthesis of aminoalkylindolizines[106]:



3-Acetyl-2-methyl(ethyl)-1-(β-dimethylaminoethyl)-indolizines, whose structure has been established by ultraviolet spectroscopy, were obtained from asymmetrically substituted carbinols of the following type: 2-methyl(ethyl)-1,5-bis(dimethylamino)-3-(2-pyridyl)-3-pentanols. The formation of the isomeric indolizines unsubstituted in the 2-position could not be observed.

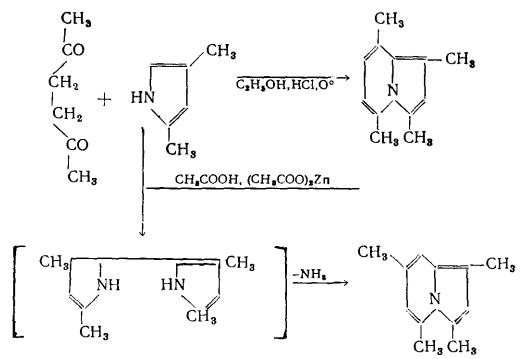
It is believed that the alkenylamines formed on dehydration of the aminomethanols are not intermediates in the conversion of the aminomethanols into indolizines, although they are converted into substituted indolizines under the same conditions. Thus 3-acetyl-1-(*p*-chlorophenyl)indolizine, mentioned above, was obtained from *cis*-1-(*p*-chlorophenyl)-1-(2-pyridyl)-3-(1-pyrrolidinyl)-prop-1-ene:



The *trans*-isomer does not cyclise under analogous conditions (refluxing for 30 min), more severe conditions being required for this purpose, and the yield of the substituted indolizine is low. In these reactions an appreciable amount of 3-acetoxy-1-(*p*-chlorophenyl)-1-(2-pyridyl)prop-1-ene is formed as a side product.

The Conversion of Alkylpyrroles into Indolizines

When 2,4-dimethylpyrrole is heated with acetonylacetone in acetic acid in the presence of zine acetate, 1,3,5,7- and 1,3,5,8-tetramethylindolizines are formed[107,108]. Later it was established that the second indolizine is formed from 2,4-dimethylpyrrole and acetonylacetone in alcoholic solution at 0°C in the presence of hydrogen chloride. It is suggested that the formation of 1,3,5,7-tetramethylindolizine proceeds via a pyrrolinylpyrrole stage[109]:

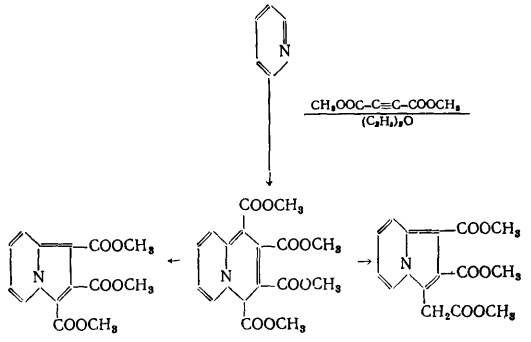


1,2,6,7-Tetraethylindolizine was obtained similarly in 24% yield from 3,4-diethylpyrrole in the presence of zinc acetate and the condensation of the same substituted pyrrole with acetonylacetone led to the isolation of 1,2-diethyl-5,8-dimethylindolizine. 3,4-Dimethylpyrrole was also converted into 1,2,6,7-tetramethylindolizine[110]. The interaction of pyrrole with hexane-2,5-dione in acetic acid containing zinc acetate leads to the formation of a mixture of various condensation products containing more than 10% of 5,8-dimethylindolizine and also substituted indole, carbazole, and other substances[111].

The Conversion of 1,2,3,4-Tetra(methoxycarbonyl)-4*H*-quinolizine into Indolizine-1,2,3-tricarboxylic Acid Esters

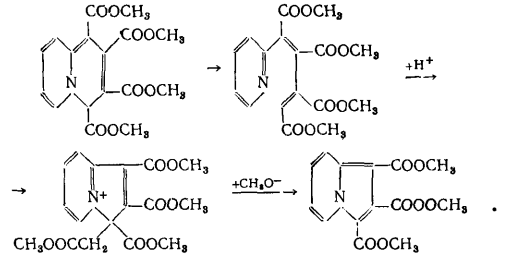
One of the substances formed in the interaction (in ethereal solution) of pyridine with acetylenedicarboxylic acid dimethyl ester is the tetramethyl ester of 4*H*-quinolizine-1,2,3,4-tetracarboxylic acid (the yellow "stable product") to which the structure of 1,2,3,4-tetra(methoxycarbonyl)-9*aH*-quinolizine was attributed previously. When this tetramethyl ester is treated with bromine and then hydrolysed, or when it is oxidised with dilute nitric acid or chromic acids, or when it is irradiated with light from a 450 W mercury lamp, the trimethyl ester of

indolizine-1,2,3-tricarboxylic acid is formed (on irradiation the yield is only 5%). When the above dihydroquinolizine is heated with phenol or formic acid, 1,2-di(methoxycarbonyl)-3-methoxycarbonylmethylindolizine is also formed[53,55,56,112-119]:

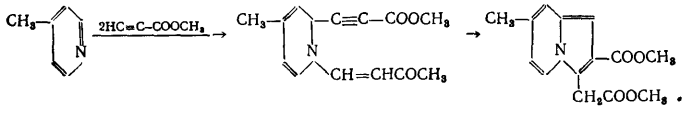


α-Picoline[120], β-picoline[115,121], isonicotinonitrile[122], and stilbazole[118,123] were introduced into the reaction with acetylenedicarboxylic acid dimethyl ester with the formation of tri(methoxycarbonyl)indolizines with the corresponding substituents in the six-membered ring.

It has been suggested that irradiation of a methanolic solution of 4*H*-quinolizine-1,2,3,4-tetracarboxylic acid tetramethyl ester (the experiment is carried out in a stream of nitrogen) leads to the opening of the 4*H*-ring with formation of a substituted α-pyridylbutadiene, which subsequently undergoes cyclisation[119]:



The substances formed in the interaction of 2-, 3-, and 4-methyl and 3,5-dimethylpyridines with methyl propiolate have been studied[124-126]. It was established (mainly by spectroscopic methods) that this involves the formation of compounds of two types: substituted cyclo-[3,2,2]azines and indolizines. The formation of 2-methoxycarbonyl-3-methoxycarbonylmethyl-7-methylindolizine from γ-picoline and a propiolate ester was observed:



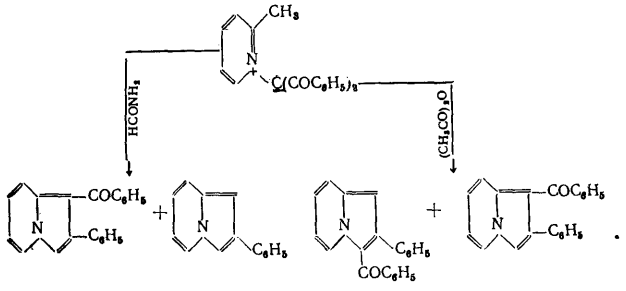
It is suggested that 2-(methoxycarbonylethynyl)-1-(β-methoxycarbonylvinyl)-4-methyl-1,2-dihydropyridine is formed as an intermediate. This method was extended to the synthesis of benzoindolizine systems[127].

The interaction of 2-phenylethynylpyridine with acetylenedicarboxylic acid dimethyl ester in acetonitrile leads to the formation of the tetramethyl ester of oxy-bis-(1-phenylmethyleneindolizine-2,3-dicarboxylic acid), whose treatment with bromine in chloroform led to a quantitative yield of 1-bromoindolizine-2,3-dicarboxylic acid dimethyl ester[128].

The Synthesis of Indolizines from Ylids

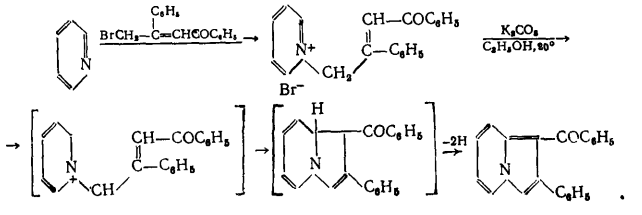
Ylids are converted into indolizines either by the cyclisation of the ylids themselves or by their interaction with acetylenic compounds, i.e. via 1,3-dipolar cycloaddition.

A mixture of 1-benzoyl-2-phenyl- and 3-benzoyl-2-phenyl-indolizines in proportions of 1 : 2 and a small amount of 2-phenylindolizine are formed from the stable 2-methylpyridinium dibenzoylmethylid when it is heated for a short time with acetic anhydride[44,79,80]. When the same ylid was refluxed in formamide, the main reaction product proved to be 1-benzoyl-2-phenylindolizine, but when the refluxing was continued only for a very short time (about 1 min), 2-phenylindolizine was obtained quantitatively:



3-Benzoyl-1-methyl-2-phenylindolizine and 3-benzoyl-1,2-diphenylindolizine were obtained in quantitative yields on refluxing 2-ethyl- and 2-benzyl-pyridinium dibenzoylmethylids respectively in acetic anhydride. The latter ylid was converted quantitatively into 3-benzoyl-1,2-diphenylindolizine when it was heated to the melting point (170–172°C) or to 200°C for 1 min in formamide[44].

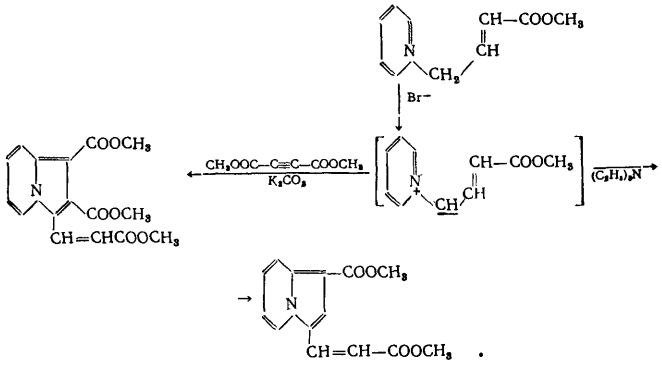
The syntheses of certain substituted indolizines where 4-bromo-1,3-diphenylbut-2-en-1-one was used for the preparation of pyridinium salts have been described. The synthesis of 1-benzoyl-2-phenylindolizine is illustrated below[129]:



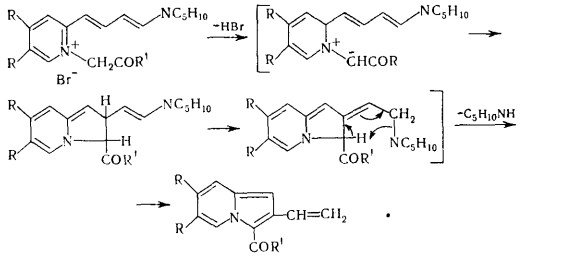
The ylid formed under the conditions of base catalysis cyclises with formation of dihydroindolizine, which is aromatised during the reaction with elimination of hydrogen.

The formation of a substituted indolizine from the analogous pyridinium salt—1-(γ-methoxycarbonylallyl)-pyridinium bromide—when the latter is heated with triethylamine apparently proceeds in a different way. Instead of the expected ester of indolizine-1-carboxylic acid, the product consisted of a 20% yield of 1-methoxycarbonyl-3-(β-methoxycarbonylvinyl)indolizine, the hydrogenation of which in the presence of palladium on charcoal led to its conversion into 1-methoxycarbonyl-3-(β-methoxycarbonylethyl)-indolizine. It is suggested that the reaction proceeds via a γ-methoxycarbonylallylid stage. This is confirmed indirectly by the formation of

1,2-di(methoxycarbonyl)-3-(β-methoxycarbonylvinyl)-indolizine from the same pyridinium salt and acetylenedicarboxylic acid dimethyl ester in dimethylformamide[88]:

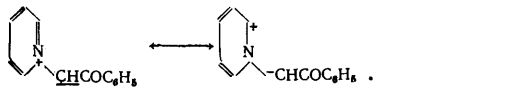


When 2,3-disubstituted quinolizinium bromide (with CH_3, C_6H_5, or H substituents) react with piperidine or morpholine, conjugated tetramethines are formed: 4,5-disubstituted 2-[4-piperidino(morpholino)buta-1,3-dienyl]pyridines. Their salts formed by reaction with bromoacetone or bromoacetophenone undergo intramolecular cyclisation when their chloroform solution is passed through a column containing alumina (Grade III activated alumina). This results in the formation of 6,7-disubstituted 3-acetyl(or benzoyl)-2-vinylindolizines[130]. The mechanism of this reaction is illustrated below:

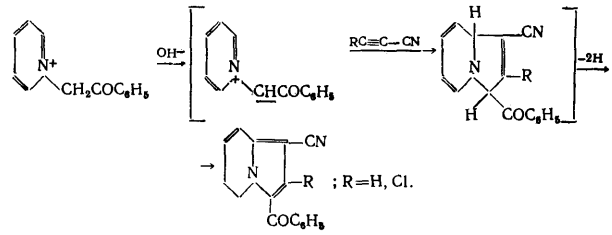


A mechanism similar to that described above was considered by Mörler and Krohnke for the formation of these indolizines[130]. The first indolizine is formed when *N*-vinylpyridine is split off from the intermediate dihydroindolizine and the second is formed via the acetylation of the dihydroindolizine in the 1-position and the elimination of piperidine. In the next communication, dealing with the study of the reactions of a salt of 4,5-disubstituted 2-(4-piperidinobuta-1,3-dienyl)piperidine and ethyl bromoacetate in the presence of acetic anhydride and triethylamine, two 6,7-disubstituted indolizines were reported: 1-(β-formylvinyl)-2-methyl- and 3-ethoxycarbonyl-1-(β-formylvinyl)-2-methylindolizines[131].

Pyridinium phenacylid[71b,132] in acetonitrile solution reacts exothermically with cyanoacetylene and also with chlorocyanoacetylene (with a 1 : 2 ylid : substituted acetylene reactant ratio), which results in the formation of substituted indolizines with a cyano-group at $C_{(1)}$ and a benzoyl group at $C_{(3)}$ in yields ranging from 5 to 25%.[133-135] Indolizines are formed from ylids and substituted acetylenes via a 1,3-dipolar cycloaddition reaction, owing to the presence of the stabilised mesomeric form of the 1,3-zwitterion of the ylid[136]:



The following explanation has been proposed for the formation of the indolizine system in the above reactions:

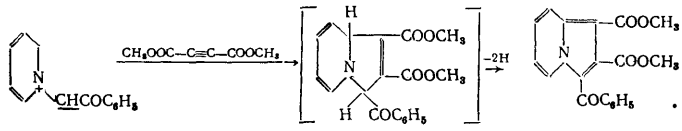


An intermediate in these reactions is an unstable dihydroindolizine, which is dehydrogenated to the final product. The substituted acetylene, which is introduced into the reaction in a molar excess, serves in this case as the hydrogen acceptor in the aromatisation of the dihydroindolizine. The formation of acrylonitrile and *trans*-β-chloroacrylonitrile as side products of these reactions was confirmed experimentally. The nitrile of 3-benzoyl-8-methylindolizine-1-carboxylic acid was obtained similarly in 10% yield from 3-methyl-1-phenacylpyridinium bromide.

3-Benzoyl-1-cyano-1,2,3,8*a*-tetrahydroindolizine, which is dehydrogenated at room temperature in the presence of palladium on charcoal to the similarly substituted 2,3-dihydroindolizine, was obtained from 1-phenacylpyridinium bromide via a stage involving the formation of an ylid. If the reaction of the ylid with acrylonitrile is carried out at an elevated temperature or for a long time, 3-benzoyl-1-cyanoindolizine, which was obtained also in the dehydrogenation of the corresponding 2,3-dihydroindolizine, is formed immediately[137].

The reaction of pyridinium phenacylid with acetylene dicarboxylic acid dimethyl ester has been investigated in fair detail. When this reaction is carried out in the presence of 5% of palladium on charcoal, 3-benzoylindolizine-1,2-dicarboxylic acid dimethyl ester is formed in 18% yield; its structure was demonstrated by converting it via acid hydrolysis and subsequent decarboxylation into indolizine-2-carboxylic acid[138]. It has been shown[139] that the use of a dehydrogenation catalyst in this reaction is not obligatory. The same indolizine was obtained in 32% yield when the reaction was performed in dimethylformamide in the presence of sodium hydride.

The intermediate in the reaction of pyridinium phenacylid with acetylene dicarbocylic acid dimethyl ester is also the corresponding dehydroindolizine, which is converted into a substituted indolizine via 1,4-elimination:



A similar mechanism has been proposed to account for the reaction of pyridine with acetylenedicarboxylic acid dimethyl ester, which leads to the formation of 1,2,3-tri(methoxycarbonyl)indolizine and 1,2-di(methoxycarbonyl)-3-[methoxy(methoxycarbonyl)methyl]indolizine[140].

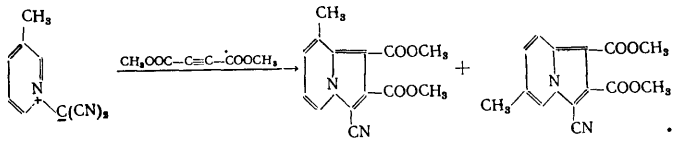
As expected, 3-substituted pyridinium phenacylids give rise to isomeric indolizines as regards the position of the substituent in the six-membered ring. 3-Benzoyl-1,2-di(methoxycarbonyl)-6-methyl(cyano)- and 3-benzoyl-1,2-di(methoxycarbonyl)-8-methyl(cyano)-indolizines were obtained in this way from 3-methyl(cyano)pyridinium phenacylids. Isomeric indolizines were also synthesised from 3,4-dimethylpyridinium phenacylid. However, as

was to be expected, 3-benzoyl-1,2,7-tri(methoxycarbonyl)-indolizine was obtained from 4-methoxycarbonylpyridinium phenacylid[135]. Ylids obtained from quaternary pyridinium salts and bromoacetone, bromoacetate esters, and bromoacetonitrile were also introduced into the reaction with acetylenedicarboxylic acid dimethyl ester. The indolizines thus obtained contain a group in the 3-position, which is linked to the methine carbon atom of the ylid. Indolizines are not formed by the above procedure from *N*-methyl(ethyl, allyl, benzyl)pyridinium salts.

When the reaction of pyridinium phenacylid with acetylenedicarboxylic acid dimethyl ester is carried out in the presence of iodine, 1,2,3-tribenzoylindolizine is formed. Bearing in mind the above mechanism, this mode of reaction has been explained by postulating the formation of dibenzoylacetylene during the reaction, although this could not be demonstrated experimentally[139]. Only 3-benzoyl-1,2-di(methoxycarbonyl)indolizine is formed from pyridinium dibenzoylmethylid and acetylenedicarboxylic acid dimethyl ester. The formation of 3-ethoxycarbonyl-1,2-di(methoxycarbonyl)indolizine from the corresponding di(ethoxycarbonyl)methylid proceeds with analogous elimination of the ethoxycarbonyl group[139].

Pyridinium dicyanomethylid is formed from pyridine and tetracyanoethylene and its interaction with acetylene dicarboxylic acid dimethyl ester at room temperature gives rise to a 48% yield of 3-cyanoindolizine-1,2-dicarboxylic acid dimethyl ester[141].

To elucidate the mode of the 1,3-dipolar cyclisation in the interaction of methylids with acetylenedicarboxylic acid dimethyl ester 3-methylpyridinium dicyanomethylid was also used:



It was established that 8- and 6-substituted indolizines are formed in this reaction in proportions of 3 : 1.[135,142]

The Synthesis of Indolizines from Heterocyclic Compounds in Their Catalytic Reactions

When furan and ammonia are passed over alumina at 350–400 °C, pyrrole and traces of indole, carbazole, and indolizine are formed[143–145]. Indolizine is also present in the products of the pyrolytic decomposition of pyridine. Octahydroindolizine could not be aromatised in the presence of palladium on charcoal or with the aid of selenium[146].

The Synthesis of a Substituted Indolizine from α-Picoline and Sulphur

Prolonged refluxing of α-picoline with sulphur leads to the formation of a substance $C_{36}H_{24}N_6S_2$, which is converted into 1,2-di(2-pyridyl)indolizine on reduction with hydriodic acid in the presence of phosphorus and into 3-nitro-1,2-di(2-pyridyl)indolizine on nitration[147].

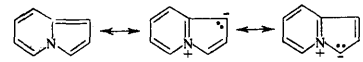
III. PROPERTIES OF INDOLIZINES

The physical and chemical properties of indolizine and its derivatives have been described fairly completely[9,10]. In the present review we shall consider mainly studies on the properties of indolizines carried out in recent years.

Electrophilic substitution reactions constitute a characteristic chemical feature of indolizines. Nucleophilic substitution—amination of indolizine with sodamide—could not be achieved[9].

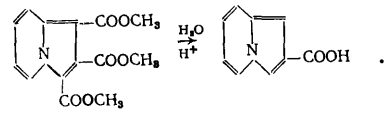
Electrophilic Substitution

Indolizine is more reactive than benzene with respect to electrophilic agents owing to the delocalisation of the lone electron pair of the nitrogen atom. An estimate of the distribution of π-electron density and of the bond orders in the indolizine molecule by the molecular orbital method[148] and also calculation of the frontal electron density in the molecule in relation to electrophilic substitution[149] have shown that its fundamental mesoforms consist of structures with maximum electron density in the 3-position and then in the 1-position[9]:



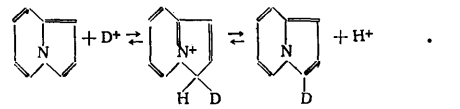
Therefore electrophilic substitution in the indolizine system should take place primarily in the 3-position and then in the 1-position; in the presence of substituents further substitution takes place in the 2-position. In electrophilic attack on indolizine substitution takes place only in the five-membered ring[150]. Substitution of the pyridine ring of indolizine cannot be achieved.

The enhanced electron density in the 3-position of the indolizine ring is indicated by the stepwise decarboxylation of indolizine-1,2,3-tricarboxylic acid. On hydrolysis (by heating with dilute hydrochloric acid) of its trimethyl ester, decarboxylation in the 1- and 3-positions takes place. Indolizine-2-carboxylic acid thus formed was decarboxylated by pyrolysing its calcium salt[53,56]:



Calculations by the LCAO-MO method[151] have shown that the 1- and 3-positions are almost equally effective in relation to electrophilic substitution with a slight preference for substitution in the 1-position. However, examination of resonance structures shows that electrophilic attack should take preferentially on the 3-position.

The calculated data were confirmed in a study of the deuteration reaction. It is suggested[152] that in the deuteration of indolizine the formation of a cation identical with a π complex constitutes an intermediate stage:



The rate of deuteration of indolizine itself in the 3-position is fives times faster than the rate of deuteration in the 1-position. Similar relative rates of deuteration in the 3- and 1-positions hold also for 2-methylindolizine. The reactivities of different positions of the

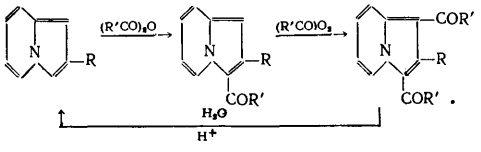
indolizine system were determined[153] with the aid of electrophilic hydrogen exchange and were compared with calculated data. The distribution of π-electron density agrees with the experimental reactivities of different positions in the indolizine system, which decrease in the sequence $3 > 1 \gg 2 > 5 \simeq 7 > 6 > 8$. Contradictions, which still remain controversial, were encountered when these results were compared with the calculated electron localisation energies.

Similar conclusions concerning the different reactivities of various positions in the indolizine ring in relation to electrophilic attack were reached on the basis of a determination by ^{1}H NMR of the degrees of protonation of the $C_{(1)}$ and $C_{(3)}$ positions in a number of methylindolizinium perchlorates in trifluoroacetic and hydrochloric acids. The protonation of indolizines without a methyl group at $C_{(3)}$ involves almost exclusively the 3-position[154]. 100% of the 3*H*-cations was detected in the protonation of 3,5-dimethyl-, 1,2,3-trimethyl-, and 1,3-dimethyl-2-phenyl-indolizines. The amounts of the 3*H*-cations and the 1*H*-cations in the case of 2,3-dimethylindolizine were 41 and 59% respectively[155].

Acylation of Indolines and the Reactions of Acylindolizines

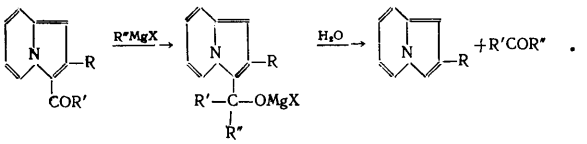
On heating with acid anhydrides in the presence of the sodium salts of the corresponding acids, indolizines are readily acylated to 3-acylindolizines[3-6,14,15,44,74,156,157]. When monoacyl derivatives are heated with the anhydride at a higher temperature, 1,3-disubstituted indolizines are formed. Acetylation of the nitrile of 2-methyl-(phenyl)indolizine-1-carboxylic acid also leads to the formation of the 3-acetyl derivative[5,14]. 3-Alkoxycarbonyl-2-methylindolizines are extremely resistant to acetylation; the yield of their 1-acetyl derivatives on acetylation with acetic anhydride in the presence of sodium acetate is only slightly more than 10%.[85]

Certain characteristic features are observed in the interaction of indolizines with acyl halides. 2-Methylindolizine is acetylated with difficulty by acetyl chloride (by the Friedel–Crafts reaction) in carbon disulphide to 1,3-diacetyl-2-methylindolizine. Acetylation of 3-acetyl-2-methylindolizine[158] and particularly 2-phenylindolizine (the phenyl group is partly acetylated)[14] proceeds more readily in the presence of aluminium chloride. In the absence of a catalyst 2-phenylindolizine does not react with acetyl chloride or bromide, but is benzoylated by benzoyl chloride in the 3-position and then in the 1-position under more severe conditions[38,44,69,79,157,159-161]. In the absence of a catalyst indolizine itself does not react with benzoyl chloride[4]:

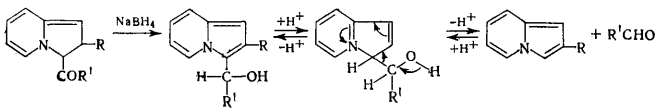


The reaction of aroylacetic acid esters with indolizine and also with 2-methylindolizine at 140°C leads to the formation of 3-(β-aryl-β-oxopropionyl)indolizines[162]. Substituted indolizines, obtained by treating indolizine with oxalyl chloride in benzene using different proportions of the reactants, have been described. 3-Carboxycarbonylindolizine and di-(3-indolizinyl)glyoxal were obtained in yields of 80% and 15% respectively[151]. 3-Ethoxycarbonyl-2-methylindolizine was synthesised from 2-methylindolizine and chlorocarbonic acid ester[85].

The acyl groups in the pyrrole ring of indolizine are readily removed by acid hydrolysis[1,3,5,14,50,76,105,106,134]. Diacyl derivatives are hydrolysed with greater difficulty than monoacyl derivatives. Acylindolizines with a nitro-[74,156] or nitroso-group[64] in the five-membered ring are not hydrolysed in this way. The acyl group is eliminated from 3-acylindolizines when they interact with organomagnesium compounds. The initial and deacylated indolizines and a ketone are present in the reaction products[48,163]:

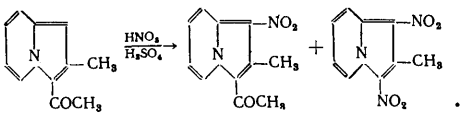


When the products of the reaction of 3-acetyl-2-methylindolizine with sodium tetrahydroborate were treated with D_2O in alcohol, 2-methylindolizine deuterated in the 3-position to an extent greater than 75% was obtained. Consequently the intermediate carbinols are readily protonated in the 3-position. These experimental findings were used to account for the mechanism of the elimination of the acetyl group from the 3-position in indolizines on treating the latter with sodium tetrahydroborate[164]:



It has been shown in many instances that the elimination of the acetyl group with the aid of sodium tetrahydroborate is selective. The acyl group is not split off from the 1-position under these conditions[164].

Nitration of acetylindolizines results in partial substitution of the acetyl group for the nitro-group. Thus nitration of 3-acetyl-2-methylindolizine in the presence of sulphuric acid leads to the formation of a mixture of 3-acetyl-2-methyl-1-nitroindolizine (59%) and 2-methyl-1,3-dinitroindolizine[156]:



3-Ethoxycarbonyl-2-methyl-1-nitroindolizine was obtained in a yield exceeding 30% by the nitration of 1-carboxymethyl-3-ethoxycarbonyl-2-methylindolizine[85]. When 3-acetyl-2-phenylindolizine is treated with iodine, the acetyl group is partly substituted by iodine and the reaction products contain 3-acetyl-1-iodo-2-phenylindolizine and 1,3-diiodo-2-phenylindolizine[48]. 3-Acylamino-2-methylindolizines are formed by the Schmidt reaction from 3-acyl-2-methylindolizines[157]. Several 1-acetamido-3-aryl-2-methylindolizines have been synthesised by this method from 1-acetyl-3-aryl-2-methylindolizines[97].

1- and 3-Acylindolizines are reduced by lithium tetrahydroaluminate to 1- and 3-alkylindolizines[67,78,82,157,165,166]. The reduction of 3-methoxycarbonyl indolizine with lithium tetrahydroaluminate leads to the formation of 3-hydroxymethylindolizine[52] and 2,3-dimethylindolizine was obtained from 3-methoxycarbonyl-2-methyl indolizine in a yield exceeding 70%.[164]

1- and 3-Acylindolizine behave differently in the reactions with hydroxylamine and phenylhydrazine. The corresponding derivatives involving the carbonyl group

are formed under the usual conditions only from 1-acylindolizines. In 1,3-diacylindolizines only the acyl carbonyl in the 1-position enters into these reactions[1,3-5,14,165]. The condensation (in the presence of alkali) of 1,3-diacetylindolizines with aromatic aldehydes leads to the formation of mono- and di-cinnamoylindolizines[1,3,14,15].

Nitrosation of Indolizines and the Reactions of Nitrosoindolizines

Direct nitrosation of indolizines with the 3-position free leads to 3-nitrosoindolizines. When the 3-position is occupied, 1-nitroso-derivatives are formed[14-16,25,27-29,64,79,167-169]. When 1-methyl-2-phenyl, 1-acetyl-5-methyl-2-phenyl-, 3-methyl-2-phenyl-, and 3-acetyl-2-phenylindolizines were nitrosated with sodium nitrite in concentrated hydrochloric acid to which glacial acetic acid or acetone had been added, the first two indolizines gave rise to 3-nitroso-derivatives and the last two gave rise to 1-nitroso-derivatives.

Careful oxidation of nitrosoindolizines with nitric, acetic, and peracetic acids converts them into nitroindolizines[64,156]. When 1-nitrosoindolizines are treated with nitric oxide in the cold, diazonium salts, stable in the solid state and in solutions, are formed in high yields. 3-Methyl-2-phenyl-1-indolizinyldiazonium nitrate was obtained in this way from 3-methyl-1-nitroso-2-phenylindolizine. After coupling it with β-naphthol, the corresponding azo-compound was isolated[168,170]:

3-Nitrosoindolizines do not react with nitric oxide even after prolonged treatment, which has not so far been explained[168]. Aminoindolizines are unstable in air and therefore cannot be used for diazotisation[50,63]. Azocyanine dyes are formed on condensation of nitrosoindolizines with heterocyclic compounds containing an active methylene group. Some of these azocyanines are used in the manufacture of photographic emulsions[171].

Formylation of Indolizines

Indolizines are formylated in the 3- and 1-positions by the Vilsmeier method using methyl- and dimethylformamides[157,165,166]. 3-Formyl-2-methylindolizine was obtained from 2-methylindolizine and then reduced by the Wolff–Kishner method to 2,3-dimethylindolizine[165]. When the formyl derivative is heated with hydrochloric acid, the formyl group is split off. 1,3-Diformyl-2-methylindolizine was obtained from 2-methylindolizine by the Reimer–Tiemann method and then reduced to 1,2,3-trimethylindolizine[165].

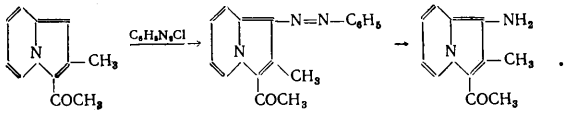
Formylation of indolizine in the presence of sodium hydrogen sulphide led to the formation of 3-thioformylindolizine[172].

Nitration of Indolizines

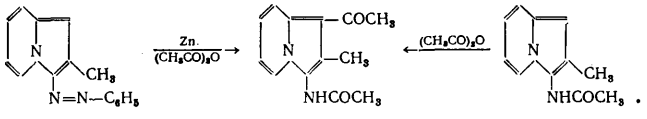
In order to suppress oxidation processes, substituted indolizines are nitrated in sulphuric acid at a reduced temperature or in nitric acid at an elevated temperature, but for a short period. Nitration results in a mixture of isomers. 2-Methyl-1-nitroindolizine and 2-methyl-3-nitroindolizine were obtained in 62 and 1.5% yields respectively by nitrating 2-methylindolizine in the presence of sulphuric acid[156]. 2-Methyl-1,3-dinitroindolizine is formed much more readily on nitration of 2-methyl-3-nitroindolizine than 2-methyl-1-nitroindolizine.

Indolizines in Azo-coupling Reactions

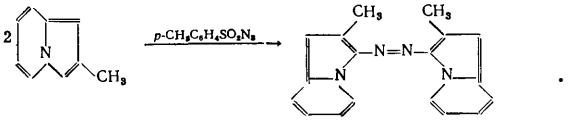
Azo-coupling of indolizine and 2-substituted indolizines involves the 3-position. When it is occupied, the 1-position is involved in azo-coupling[4,68-71,157,167]. 3-Acetyl-2-methyl-1-phenylazoindolizine was obtained by coupling phenyldiazonium chloride with 3-acetyl-2-methylindolizine and its catalytic reduction gave rise to 3-acetyl-1-amino-2-methylindolizine, which is unstable in air[167]:



The reduction of 2-methyl-3-phenylazoindolizine with zinc in acetic anhydride led to the isolation of 3-acetamido-1-acetyl-2-methylindolizine, which is resistant to acid and alkaline hydrolysis and which is formed also on acetylation of 3-acetamido-2-methylindolizine[120]:



3,3′-Azobis(2-methylindolizine) is formed in the reaction of 2-methylindolizine with tosyl azide[173]:

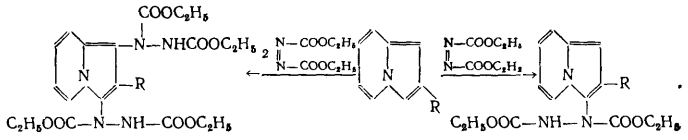


Similar azo-compounds coupled at the 1-position in the indolizine ring have been obtained from 2,5-dimethyl- and 3-methyl-2-phenyl-indolizines. 2-Phenylindolizine does not react with tosyl azide even on heating[174]. It has been confirmed[175] that 3,3′-azobisindolizines are formed from 2-methylindolizine and from 1,2-dimethylindolizine, both on treatment with tosyl azide and with picryl azide in ethyl acetate. Under the same conditions, 1,1′-azobis-(2,3-dimethylindolizine) is formed from 2,3-dimethylindolizine. This condensation takes place particularly readily with 2-methyl- and 1,2-dimethyl-indolizines. Fast dyes for polyamide and polyester fibre with tints ranging from yellow to violet have been found among 3-(1-indolizinylazo)-2-phenylindoles, 2,3-disubstituted in the indolizine ring, and 2-substituted 3-(3-indolizinylazo)-2-phenylindoles[176].

Condensation of Indolizines with Certain Dienophiles and with Azodicarboxylic Ester

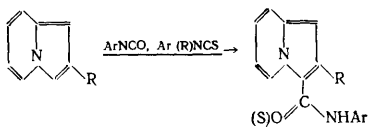
Adducts formed by indolizines with malic anhydride[123,177] and with quinone[4] have been described. 2-Phenyl(methyl)-indolizine is involved in a Diels–Alder type of reaction in benzene at room temperature with the diethyl ester of azodicarboxylic acid, forming a monoadduct—the diethyl

ester of [2-phenyl(methyl)-3-indolizinyl]hydroazodicarboxylic acid, while on refluxing a di-adduct is formed[178]:

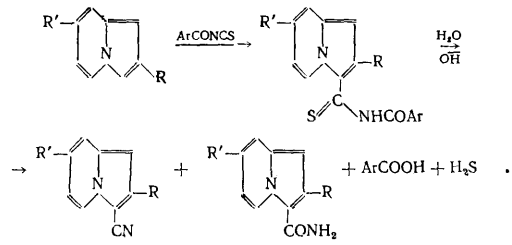


Similar addition products were obtained from 1-methyl-2-phenyl-, 3-methyl-2-phenyl-, and 2,3-dimethylindolizines. As a rule, the 3-adducts are formed more readily and in higher yields than the 1-adducts.

The carbamoylation and thiocarbamoylation of indolizines can be included among reactions of a similar type. When equimolar amounts of 2-methylindolizine and phenyl isocyanate, formed on decomposition of benzoyl azide under these conditions, are refluxed in toluene, the *N*-phenylamide of indolizine-3-carboxylic acid is obtained[179]. The thiocarbamoyl group is introduced similarly into the 3-position of 2-methyl- and 2,7-dimethyl-indolizines when these interact with isothiocyanates[180]:

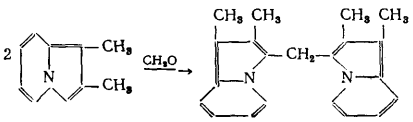


N-Aroylthioamides of the corresponding indolizine-3-carboxylic acids were synthesised from 2-methyl-, 2-aryl-, 2,7-dimethyl-, and 2-aryl-7-methyl-indolizines and aroyl isothiocyanates[181,182]; on being refluxed in an alkaline alcoholic solution, they give rise to nitriles and amides of indolizine-3-carboxylic acids (in yields up to 15%):[183]

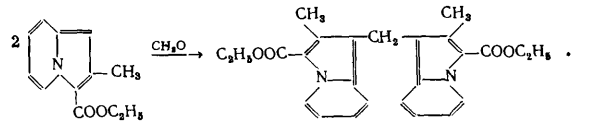


Alkylation of Indolizines

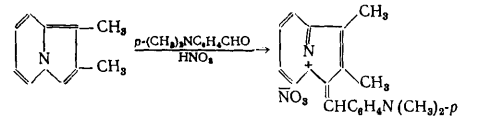
Alkyl groups, which may be substituted by functional groups, can be introduced into the 3- and 1-positions of indolizines in several ways. (3-Benzoyl-1-indolizinyl)-acetic acid was synthesised by the condensation of 3-benzoylindolizine with diazoacetic ester[184]. Condensation of indolizines containing free 1- or 3-positions with formaldehyde and other aldehydes leads to diindolizinylmethanes[1,3,4,93,105,157,165]. Di-(1,2-dimethyl-3-indolizinyl)-methane was obtained in a yield exceeding 90% from 1,2-dimethylindolizine and 40% formaldehyde solution[185]:



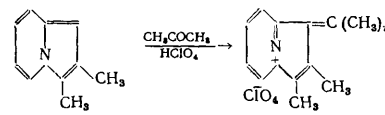
A similar condensation product involving the 1-positions of the indolizines rings was obtained from 2,3-dimethylindolizine[165]. The condensation of 3-ethoxycarbonyl-2-methylindolizine with formaldehyde gave a 75% yield of di-(3-ethoxycarbonyl-2-methyl-1-indolizinyl)methane[85]:



The condensation of 1,2- and 2,3-dimethylindolizines with *p*-dimethylaminobenzaldehyde in alcoholic solution in the presence of nitric acid led to the formation of 1,2-dimethyl-3-(*p*-dimethylaminobenzylidene)indolizinium and 2,3-dimethyl-1-(*p*-dimethylaminobenzylidine)-indolizinium nitrates respectively[37]:



A similar dye was synthesised by the condensation of 2-methylindolizine hydriodide with *p*-dimethylamino-benzaldehyde[36]. Methine derivatives of indolizines have been synthesised by condensing them with aromatic ketones containing the *p*-dimethylamino-group in one of the benzene rings[37] and also with aliphatic ketones. The condensation of 2,3-dimethylindolizine with acetone in the presence of perchloric acid led to the isolation of 1-isopropylidene-2,3-dimethylindolizinium perchlorate[165]:

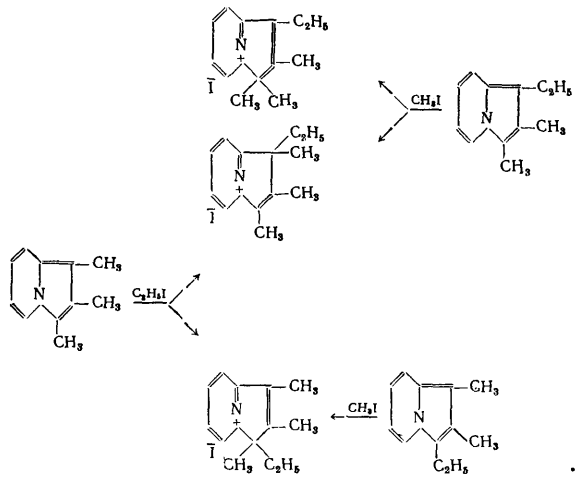


The products of the condensation of 2-aryl-1-methylindolizines with *p*-dimethylaminobenzaldehyde and with di-(*p*-dimethylaminophenyl) ketone were isolated as the perchlorates or the tetrafluoroborates[186].

The condensation of 5-methyl-2-phenylindolizine with *NN*-dimethylacetamide in the presence of phosphoryl chloride results in the formation of a mixture of 1- and 3-(α-dimethylaminoethylidene)indolizines, which were isolated as the perchlorates. After treating a mixture of these perchlorates with sodium hydroxide, 1-acetyl-5-methyl-2-phenylindolizine and an enamine [3(α-dimethylaminovinyl)-5-methyl-2-phenylindolizine] were obtained. If there is no substituent causing steric hindrance at $C_{(5)}$ in the indolizine ring, then condensation with *NN*-dimethylacetamide proceeds almost wholly with formation of the 3-(α-dimethylaminoethylidene) derivative[187].

The interaction of indolizines substituted by alkyl groups in the five-membered ring with certain alkyl iodides has been studied[10,36]. The alkyl halide adds to 1,2,3-trialkylindolizine with formation of an indolizinium salt, the alkyl group entering both the 3- and 1-positions.

In 2,3-dialkylindolizines the alkyl group enters the 3- and 1-positions:



3-Phenacyl-2-phenylindolizine was obtained from 2-phenylindolizine and bromoacetophenone semicarbazone in the presence of triethylamine[188]. The reaction of 2-methylindolizine with ethyl iodoacetate in the presence of aluminium chloride results in the formation of a mixture of 3-ethoxycarbonylmethyl-2-methylindolizine, 1,3-di(ethoxycarbonyl methyl)-2-methylindolizine, and the initial indolizine. The attempt to introduce the ethoxycarbonylmethyl group into 2-methylindolizine with the aid of bromoacetic and diazoacetic esters was unsuccessful[161].

2,3-Dimethylindolizine was aminomethylated via the Mannich reaction. On treatment with dimethylamine, 2,3-dimethyl-1-dimethylaminomethylindolizine was obtained[165]. A number of similar 3-aminomethyl-1,2-diphenylindolizines substituted in the amino-group have been described[189]. 1-Aminomethyl derivatives with dimethyl- and diethyl-amino-groups and also with an *N*-pyrrolidinyl substituent have been synthesised from 3-alkyl-2-phenylindolizines[190,191]. A number of 1,3-bis-(dialkylaminomethyl)-2-phenylindolizines were synthesised from 2-phenylindolizine for pharmacological study[192]. The synthesis of unsubstituted aminomethylindolizines is difficult. Reduction of the amide of indolizine-2-carboxylic acid (which was obtained by heating the methyl ester of this acid with ammonia in methanol at 155°C) with lithium tetrahydroaluminate led to the isolation of an unstable substance to which the structure of 2-aminomethylindolizine was attributed on the basis of infrared and NMR spectra[52]. 1-Aminomethylindolizine is also very unstable; it was characterised as the *N*-acetyl derivative[50]. 3-(1-Hydroxy-2-dimethylaminoethyl)-2-phenylindolizine was obtained in a low yield by the reduction of *NN*-dimethyl-(2-phenyl-3-indolizinyl)glyoxylamide with lithium tetrahydroaluminate[43]. The reduction of the nitrile of 2-methylindolizine-7-carboxylic acid with lithium tetrahydroaluminate led to the isolation of 7-aminomethyl-2-methylindolizine[52].

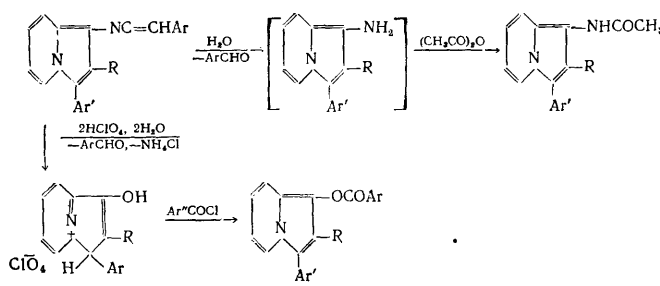
2-Hydroxymethyl-, 3-hydroxymethyl-, and 6-hydroxymethyl-2-methyl-indolizines were obtained in fairly high yields by the reduction of the corresponding indolizinecarboxylic acid esters with lithium tetrahydroaluminate[52]. However, the reduction of the ethyl ester of 2-methylindolizine-1-carboxylic acid with $LiAlH_4$ in tetrahydrofuran led to the isolation of only one product—1,2-dimethylindolizine[52].

The methyl group in the 5-position of the indolizine ring system is analogous to the methyl group of α-picoline. When 5-methylindolizine and 5-methyl-2-phenylindolizine are treated with butyl-lithium and then with a carbonyl compound, the corresponding 5-(β-hydroxyalkyl) derivatives are formed[193]. After treating 5-methyl-2-phenylindolizine with butyl-lithium and then with dimethylbenzamide, 5-phenacyl-2-phenyl-indolizine was obtained. 5-Formylmethyl-2-phenylindolizine was synthesised similarly using dimethylformamide. The same reactions were achieved also with 5-methylindolizine[194].

Amino- and Hydroxy-indolizines

1-Aminoindolizines, which are formed on reduction of 1-nitroso- and 1-nitroindolizines, could not be isolated since they are unstable in air[113,167]. 1-Amino-2-phenylindolizine hydrochloride, obtained by the reduction of 1-nitro-2-phenylindolizine with hydrogen in the presence of palladium on charcoal, is unstable like the base itself[63]. 3-Acetamido-1-acetyl-2-methylindolizine[157], 1-acetamido-(propionamido, benzamido)-2,3-dimethyl- and 1-acetamido-(propionamido, benzamido)-2,3-diphenyl-indolizines[67], and 1-acetamido-2-phenylindolizine were synthesised in various ways. The last compound is resistant to alkali, but on acid hydrolysis is readily converted into 1-hydroxy-2-phenylindolizine[50,63]. The unstable hydrochloride of 1-hydroxy-2,3-diphenylindolizine was obtained by the hydrolysis of 1-benzamido-2,3-diphenylindolizine in the presence of hydrochloric acid[50]. The conversion of 1-amino-2-phenylindolizine into 1-acetamido-2-phenylindolizine and the acid hydrolysis of both indolizines to the unstable 1-hydroxy-2-phenylindolizine have been described[63].

1-Azomethines, formed when 2-acylpyridines interact with aromatic aldehydes in acetic acid in the presence of ammonium acetate, are hydrolysed in the presence of acetic anhydride with formation of 1-acetamidoindolizines. After such 1-azomethines have been heated for a long time with 70% perchloric acid, 1-hydroxyindolizinium perchlorate can be isolated and then benzoylated by the Schotten–Baumann method at the hydroxy-group to give the benzoyl derivative[97,102]:



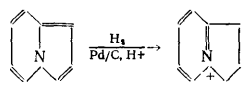
1-Hydroxy-3-phenyl-(*p*-chlorophenyl, *p*-anisyl)-indolizinium and 1-hydroxy-2-methyl-3-phenyl-(*p*-chlorophenyl, *p*-anisyl)indolizinium *p*-nitrobenzoates were obtained in this way.

Reduction and Oxidation of Indolizines

Indolizine[9] and substituted indolizines[66] are not reduced by zinc in acid[1] and on hydrogenation under the usual conditions in the presence of palladium on charcoal. Alkylindolizines are hydrogenated in the presence of

Raney nickel or the Adams catalyst at room temperature to 5,6,7,8-tetrahydro-derivatives and on heating to octahydroderivatives[9,11,14,15,25,54-56,66,92,109,114,195,196]. When 6-ethylindolizine was hydrogenated in glacial acetic acid on a platinum oxide catalyst (at 20°C and 7 atm), 6-ethyloctahydroindolizine was obtained in 80% yield[54]. The hydrogenation of 3-acetyl-2-methyl(phenyl)indolizines in the presence of the Adams catalyst at room temperature also stops at the stage of the 5,6,7,8-tetrahydroderivatives[15,196]. 1-(ω-Aminoalkyl)-2-phenylindolizines are not hydrogenated on a palladium catalyst, while on Raney nickel the reduction also involves the six-membered ring and yields the tetrahydroderivatives[56].

However, in 2*N* hydrobromic acid in the presence of palladium on charcoal indolizine is hydrogenated in the five-membered ring with formation of 1,2-dihydro-3*H*-indolizinium bromide in 85% yield:



It is suggested that in an acid solution there exists a mesomeric form of indolizine, which contains a pyridine ring conjugated with a double bond in the five-membered ring and that this species is hydrogenated[197].

Alkylindolizines are readily oxidised even by atmospheric oxygen[1,2]. Electrophilic substituents in the five-membered ring stabilise indolizines with respect to oxidants; indolizine-1,2,3-tricarboxylic acid is not oxidised by either nitric or chromic acid[48,55,56]. The final product of the oxidation of indolizines by peracetic acid or hydrogen peroxide in acetic acid is picolinic acid *N*-oxide or its homologues[55].

Physiological Properties of Indolizines

The research on indolizines is to a great extent concerned with the study of their physiological properties in addition to synthetic and theoretical investigations of this heterocyclic system. The hydrogenated indolizine system is contained in strychnine, securinine, and veratrine alkaloids: cevine, germine, and protoverine. There are some similarities between indolizines and serotonine.

It has been reported that certain alkylindolizines resemble convulsants in their physiological action; they paralyse muscular and respiratory activity[198]. Mannich bases obtained from 1,2-diphenylindolizine, formaldehyde, and ephedrine as well as a deoxy-analogue of the last compound have a depressant effect on the central nervous system[199]. 3-Dialkylaminomethyl-1,2-diphenylindolizines[192,200] and 1-aminoalkyl-2-phenylindolizines[66,190,191] also influence the central nervous system. 2-Furylindolizines exhibit antimicrobial activity[169]. Indolizine-1-acetic acid is an analgesic. 3-Acetyl(benzoyl)-1-(α-carboxyethyl)indolizines have been patented as analgesic and anti-inflammation agents[61].

3-Benzoylindolizine-1-acetic acid (the structural analogue of heteroauxin) exhibits an auxin-like activity[184]. β-(1-Indolizinyl)alanine is a tryptophan antimetabolite[201]. 1-Carboxymethyl-3-(*p*-chlorobenzoyl)-7-methoxy-2-methylindolizine and 3-carboxymethyl-1-(*p*-chlorobenzoyl)-6-methoxy-2-methylindolizine exhibit anti-inflammatory activity but are less effective than indomethacin [1-(*p*-chlorobenzoyl)-5-methoxy-2-methylindole] although less toxic than the latter[161]. It has been established that 2-arylindolizines are not carcinogenic[28].

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Structure and Properties of Heat-resistant Polymers

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The influence of the chemical structure of heat-resistant aromatic polymers on their physical properties is discussed mainly in relation to mechanical properties. Methods for determining the heat resistance of polymers and their mechanical performance are described, and the calculation of the principal physical characteristics from the chemical structure of the repeating unit is explained. A detailed account is given of the effect of chemical structure on the glass point of heat-resistant aromatic polymers and on relaxation transitions within the temperature range of the vitreous state. A list of 131 references is included.

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I. INTRODUCTION

The multitude of scientific publications appearing during recent years are testimony to the attention paid by specialists to the synthesis and the properties of heat-resistant polymers. A widely used route to such polymers is the synthesis of various polyheteroarylenes. Saturation of the polymer chain with aromatic ring systems and ladder-like fragments leads to increases in both skeletal and kinetic rigidity of the macromolecules, and hence to significant rises in the glass point and in the modulus of elasticity, with improvements in the strength and other properties of the polymer systems.

We attempt to summarise published information on the effect of the chemical structure and the supermolecular structure of the broad class of polyheteroarylenes and certain other heat-resistant polymers on their various physical properties, including mechanical (relaxation and strength), electrical, etc. properties. Special attention is paid to the nature of the heat resistance of polymers. These problems have recently been dealt with in several monographs [1-7] and reviews [8-10]. The present Review, therefore, will discuss the most recent research results, not covered in the above publications.

II. CHARACTERISTICS OF THE HEAT RESISTANCE OF POLYMERS

Before discussing results we must examine the very concept of the "heat resistance of polymers". According to one definition [11] "heat resistance is the ability of a polymer to retain at high temperatures the hardness necessary for the performance of articles made from it". In practice heat resistance is often measured in terms of certain temperatures, at which deformation of the polymer by a strictly defined amount occurs under a specified load (e.g Vicat or Martens heat resistance). With such a measure it is not always borne in mind that actual softening† of a material (i.e. loss of heat resistance) may take place not only at the glass point, determined under certain mechanical conditions, but also at any point within a range of temperatures if other stresses are applied.

In this connection Korshak [1,2] understands by heat resistance the "limiting temperature at which a polymer loses its mechanical strength under the influence of a particular load". It is very significant that this limiting temperature is influenced not only by the magnitude but also by the duration of the mechanical stress. Small stresses acting for a long time may produce the same breakdown of the material as do large stresses, when softening or fracture takes place rapidly. The same applies also to the temperature: fracture or softening occurs after a longer time at a comparatively low temperature than at a comparatively high temperature under otherwise similar conditions. The heat resistance of a plastic, i.e. retention of shape and integrity by the solid, can therefore be characterised physically either by a time [12] (under specified mechanical and thermal conditions),

†Since the softening of a material may present two different aspects—softening of a solid (i.e. an abrupt decrease in Young's modulus) and the appearance of fluidity—the concept of "softening temperature" requires refinement. If the decrease in Young's modulus is important, the softening temperature of a vitreous polymer coincides with the glass point, and that of a crystalline polymer with the melting point. If, however, the appearance of fluidity is significant, the softening temperature is usually defined as that at which a substance in a capillary begins to flow under its own weight, and then coincides with the pour point (in the absence of degradation). If a solid polymer (vitreous or crystalline) undergoes chemical degradation when heated, its softening temperature coincides with the beginning of intense thermal degradation.

by a maximum performance temperature (with a definite mechanical constraint acting for a specified period), or by a maximum permissible stress (acting under specified temperature and time conditions).

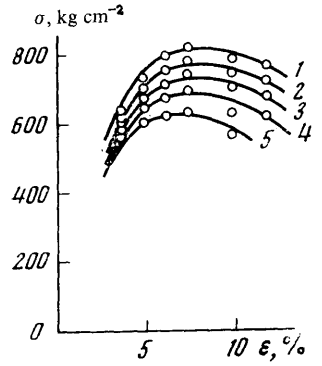


Figure 1. Isochronous dependence of stress σ on deformation ϵ for a polyimide of anilinefluorene and oxy-4,4′-diphthalic dianhydride (POI-10) at 130°C for different relaxation times t_r (min): 1) 1; 2) 3; 3) 10; 4) 60; 5) ∞.

If the conditions of service of the material require that its deformation should not exceed a specified value, the heat resistance will be characterised by the time of retention of shape t_{sh}, during which deformation under load (under certain temperature conditions) does not exceed this specified value. If, however, the stress in a material must not fall (owing to relaxation) below a required value, the heat resistance will be characterised by the time t_r during which this condition is satisfied (under specified temperature conditions).

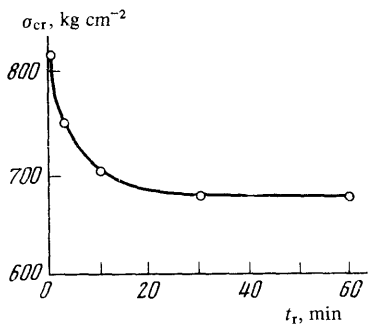


Figure 2. Dependence of σ_{cr} on t_r for POI-10 at 130°C.

To determine the maximum stresses that can be retained in a polymer for a specified time after the beginning of relaxation it is necessary to plot the stress σ against the deformation ϵ, when each curve corresponds to a definite duration of relaxation, i.e. is an isochronous dependence. Such relations usually pass through a maximum (Fig. 1). This maximum stress σ_{cr} depends significantly, of course, on the duration t_r of relaxation, as is illustrated by Fig. 2 for the polyimide of anilinefluorene and the dianhydride of the 3,3′,4,4′-tetracarboxylic acid of diphenyl ether. The dependence of σ_{cr} on t_r shows a monotonic decrease and conforms closely to Kohlrausch's equation.

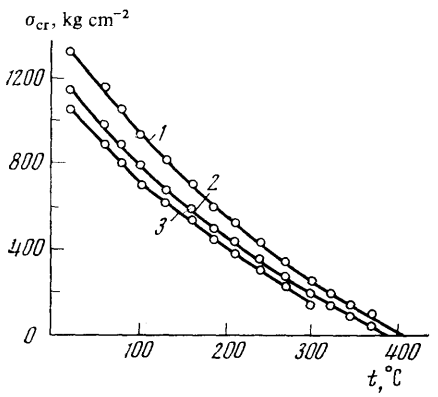


Figure 3. Temperature dependence of σ_{cr} for POI-10 after different relaxation times: 1) 1 min; 2) 60 min; 3) ∞.

From this equation we can determine the relaxation parameters, among which the most interesting is the maximum stress $\sigma_{cr,\infty}$ produced in a polymer by the completion of relaxation. It is a structural characteristic of the material, depending only on the chemical structure and the supermolecular structure. The temperature dependence of σ_{cr} determined for different relaxation times provides a complete description of the heat resistance of the polymer material (Fig. 3). These graphs also enable the period t_r of retention of the relaxing stress to be determined as a function of lg σ_{cr}. When the times are short these relations are linear (Fig. 4) and are described by the equation

$$t_r = A\sigma_{cr}^{-(\alpha_0 - \kappa T)} e^{U/RT}, \qquad (1)$$

where A, α_0, κ, and U are parameters of the material, R is the universal gas constant, and T is the absolute temperature. A more complicated relation applies for longer relaxation times [12]. The temperature dependence of $\sigma_{cr,\infty}$ and the dependence of t_r on σ_{cr} have since been used by several workers in assessing the influence of the chemical structure of a polymer on its heat resistance (see below).

Lengthy experiments are required to characterise heat resistance by the measurement of stress relaxation throughout the ranges of possible temperatures and deformations for each polymer. Such a determination should therefore be reserved for assessing the heat resistance only of the most promising individual representatives of a given class of polymers. More rapid assessment can be made by a widely used method [13-16] in which stress relaxation is examined under non-isothermal

conditions. For this purpose prismatic monolithic specimens of the polymer are placed between the working plates of a relaxometer and are deformed a certain amount, after which the temperature is raised linearly with time. In fixed specimens under such conditions, of course, compressive stresses arise as a consequence of the tendency to thermal expansion. With rise in temperature the stress increases to a certain limit, after which it falls as a result of accelerating relaxation, to reach zero at the glass point. By imposing different initial deformations on a specimen, we can obtain a series of such relaxation curves, each with its maximum (Fig. 5).

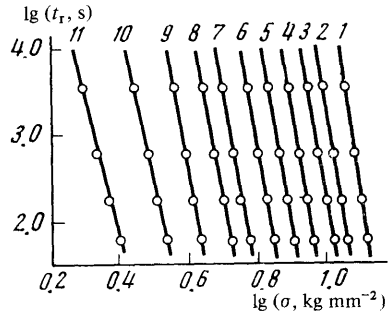


Figure 4. Dependence of lg t_r on lg σ_{cr} for POI-10 at various temperatures (°C): 1) 20; 2) 60; 3) 80; 4) 100; 5) 130; 6) 160; 7) 185; 8) 210; 9) 240; 10) 270; 11) 300.

The geometrical locus of these maxima delimits the region of stresses and temperatures within which the polymeric material remains effective, i.e. preserves heat resistance. The curve bounding the region of effectiveness obeys the equation

$$\ln \frac{\sigma}{\sigma'_\infty} = \frac{U_{r,0} - \gamma_r \sigma}{RT}, \qquad (2)$$

where $U_{r,0}$ is the initial activation energy of relaxation, and γ_r and $\sigma'_\infty = E\alpha\tau_{r,0}$ are parameters of the material, in which E is the Young's modulus, $\tau_{r,0}$ the pre-exponential factor in the temperature dependence of the stress-relaxation time, and $\alpha = \beta K$ the rate of deformation due to thermal expansion, β being the rate of temperature rise with time and K the coefficient of linear thermal expansion.

Experiment shows that, with a rate of heating of ~1.50 deg min^{-1}, the curve bounding the performance region almost coincides with the temperature dependence of σ_{cr} (Fig. 2) determined at a relaxation time t_r = 5 min. At longer relaxation times the bounding curves will, of course, be displaced to lower temperatures, but not very greatly (as in Fig. 3).

A thermomechanical method is also widely used for assessing the heat resistance of polymers. It is noteworthy that, over quite a wide range of molecular weights, many heat-resistant polymers do not exhibit rubberlike elasticity, passing directly from a vitreous solid to a viscous fluid when heated. In this case the temperature dependence of deformation (the thermomechanical curve) was described[17,18] in terms of Maxwell's model of a viscoelastic material. With a non-linear rise in temperature with time

$$T = a/(b - t), \qquad (3)$$

where a and b are constants, the thermomechanical curve will be represented by the equation

$$\varepsilon = \frac{\sigma a R}{E\tau_{r,0}U_r} e^{-U_r/RT}, \qquad (4)$$

in which ϵ is the relative deformation, σ is a constant stress, $\tau_{r,0}$ and U_r are parameters characterising the relaxation properties of the polymeric material, and E is the Young's modulus.

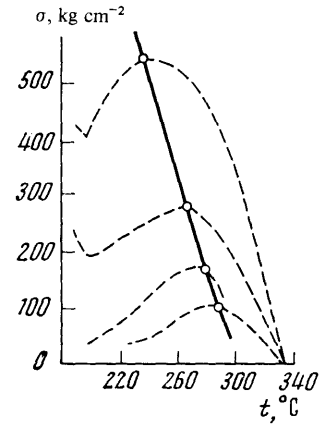


Figure 5. Performance range of polyamide of terephthalic acid and anilinephthalein.

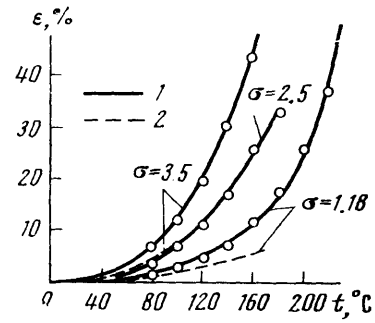
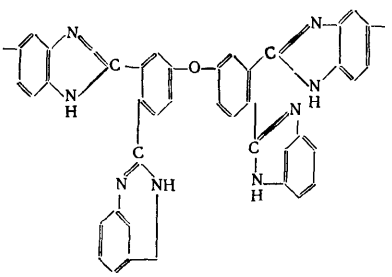


Figure 6. Thermomechanical curves (σ in kg mm^{-2}) for polyester of isophthalic acid and phenolphthalein having different structures: 1) fibrillar; 2) globular.

Fig. 6 shows thermomechanical curves obtained when films of a globular and a predominantly fibrous polyester of isophthalic acid and phenolphthalein are subjected to uniaxial extension. Only slight deformation is possible in the former polymer, but quite large deformation in the latter, which can thus pass into a viscous fluid under the

influence of mechanical stress. Experiments and calculations showed that the activation energy of relaxation U_r is rather larger for a globular than for a fibrous structure.

The relative simplicity of the relaxation process is indicated by the adequate description of the transition from solid to viscous fluid by Maxwell's method, i.e. by means of a single relaxation time that depends on temperature and stress. Softening in other heat-resistant systems, e.g. in various polybenzazoles, does not take place by one simple mechanism[19]. Fig. 7 shows thermomechanical curves (plotted as lg ϵ against $1/T$) for the polybenzimidazole



Since the relation is non-linear, relaxation is not described in this case by the usual temperature dependence of a single relaxation time.

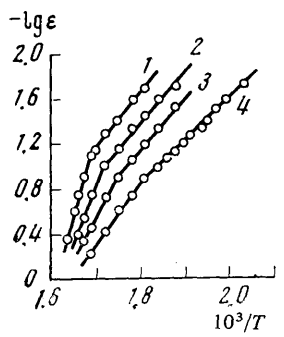


Figure 7. Thermomechanical curves for polybenzimidazole determined under different stresses (kg cm^{-2}): 1) 100; 2) 200; 3) 300; 4) 400.

In characterising the mechanical performance of polymers in general and their heat resistance in particular we must bear in mind the occurrence of several transitions at lower temperatures in addition to the main relaxation corresponding to transition from a vitreous solid into a state of rubberlike elasticity or of viscous flow. They are not revealed by the usual dynamic (mechanical and electrical) test methods but by examination of the relaxation properties of polymers under static conditions. Heat-resistant rigid-chain polymers are the most suitable subjects, since they exist in a vitreous state over an extremely wide temperature range, within which forced rubberlike elasticity develops: in other words, such polymers do not soften over a wide temperature range and do not exhibit brittle fracture.

These relaxation transitions were discovered earlier by Lazurkin[20] in a study of the temperature dependence of the limit of forced rubberlike elasticity for several polymer glasses and by Bartenev[21,22] in an investigation of the temperature–time dependence of strength for several systems over a wide temperature range. Transition from one substate to another entailed a change not only in its durability but also in its stress dependence. Thus, even before reaching the brittle point, the region of the vitreous state can be subdivided into at least two substates, in which different types of relaxation processes occur.

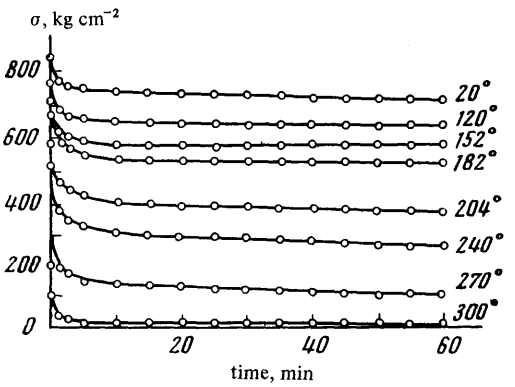


Figure 8. Stress-relaxation curves for polyester of terephthalic acid and phenolphthalein (ϵ = 4.4%).

Relaxation transitions detected by static methods of investigation are also very clearly developed in heat-resistant polymers. They have been studied[12,14,15,23] by examining the relaxation of stress at constant deformation under isothermal conditions. This yields a series of relaxation curves—the time dependence of stress—each corresponding to a certain chosen temperature. Fig. 8 shows that the relaxation curves are quite close together at low temperatures, and begin to shift rapidly down towards low stresses only after a certain temperature has been reached. A clearer idea of the temperature dependence of relaxation properties can be obtained from several properties, of which the simplest and most convenient is the relative decrease in stress after a specified relaxation time

$$\beta = \frac{\sigma_d - \sigma_t}{\sigma_d}, \qquad (5)$$

where σ_i is the stress on completion of deformation and σ_t the stress after relaxation for a certain time (e.g. 1 h).

The temperature dependence of $1/\beta$ is very characteristic (Fig. 9): it remains constant over a wide temperature range, after which it drops sharply, and then decreases smoothly with rise in temperature, to reach unity at the glass point. This means that the range of the vitreous state for a given system can be subdivided into two regions, differing in the temperature dependence of the relaxation parameters. At the lower temperatures the rate and extent of relaxation are relatively insensitive to temperature. The higher-temperature region shows a

sharp acceleration of relaxation processes, which is typical of many of the polymers studied earlier, not possessing high-glass points.

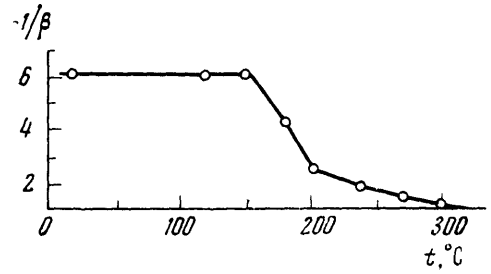


Figure 9. Temperature dependence of β^{-1} for polyester of terephthalic acid and phenolphthalein.

Without discussing the mechanism of the transition from one substate to the other, we note that such transition must be taken into account for an objective assessment of the heat resistance of a polymer. The glass point is usually regarded as the upper temperature limit of heat resistance: i.e. it is assumed that the polymer can be used right up to this temperature. This may be valid under very small loads for very short times. But even that is not the point. If a polymer material is functioning under variable temperatures, its transition from one substate to another, involving a sharp acceleration of relaxation processes, may lead to a complete loss of performance at temperatures far below the glass point. This is apparent, for example, in an abrupt increase in the coefficient of friction and in the seizing of moving parts[24]. Thus the zone of stable performance lies in the temperature range corresponding to the first substate, in which the rate of relaxation is insensitive to temperature. The real temperature range within which heat resistance is maintained therefore extends only to a temperature far below the glass point.

The above features are evident when the heat resistance of polymers is investigated by the measurement of stress relaxation. Prolonged creep tests under various loads must also be made for a more detailed assessment of the mechanical properties of heat-resistant polymers and for a comparison of their deformation behaviour under load. The isochronous stress–deformation curves obtained from these tests enable the rigidity of the systems to be judged more objectively[25].

III. CHEMICAL STRUCTURE AND PROPERTIES OF HEAT-RESISTANT AROMATIC POLYMERS

Before discussing the effect of the chemical structure of heat-resistant polymers on their properties, we must consider briefly the processing of such systems. Heat-resistant polymers whose glass point lies considerably below the temperature at which they begin to decompose can be processed[26] by the usual methods of injection moulding at high temperatures. The properties of monolithic specimens of poly(phenylene sulphide) have been reported[27]: specimens obtained by injection moulding possess moderate breaking stress (770 kg cm^{-2}), and extremely slight deformability (ϵ_r = 3%), but a considerable bending modulus of elasticity (E = 42 200 kg cm^{-2}); the maximum temperature limit to the performance of poly(phenylene sulphide) is assumed[27] to be 260°C.

Application of the usual methods of injection moulding and hot extrusion to process into monolithic articles highly heat-resistant polymers, in particular polyheteroarylenes, is made extremely difficult by the intensity of the accompanying thermal degradation and cross-linking. However, monolithic articles can be obtained from such polymers if processing is conducted below the limiting temperature at which thermal degradation takes place. By using high pressures and extruding at a temperature a few dozen degrees below that at which loss in weight begins we can obtain monolithic specimens from such heat-resistant systems as polytriazoles and polypyrazoles[28], polyphenylenes[29], aromatic polyimides[30–32], etc. This enables us to examine the effect of the chemical structure of polyheteroarylenes on their mechanical properties, in particular to specify the effect of the heterocycle.

If the heterocycle occupies a comparatively small volume, as e.g. in the case of poly(oxydi-*p*-phenylene–1,3,4-oxadiazole), appreciable crystallisation may occur, which in turn will tend to extend the performance range. With a more bulky ring system, e.g. poly(oxydi-*p*-phenylene–4-phenyl-1,2,4-triazole), the kinetic rigidity of the chain is increased, but crystallisation does not take place, the former factor tending to increase the performance range, and the latter to diminish it. Although the two effects are mutually competitive, experience shows that, with polyoxadiazoles and polytriazoles, crystallisation leads to a greater extension of the stress and temperature limits within which the polymer is effective. Competition between two processes—degradation and cross-linking—also occurs, however, if the polymer undergoes physical changes during processing. Cross-linking may have a favourable influence, promoting consolidation of the specimen at temperatures below the softening point (under the influence of high pressures). Thus the processing of poly-*p*-phenylene-1,2,3-triazole at 360°C yields monolithic specimens, whose performance range extends far above the processing temperature (Fig. 10).

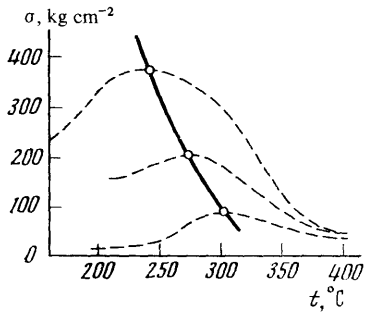


Figure 10. Performance range of poly-*p*-phenylene–1,2,3-triazole.

An especially interesting heat-resistant polymer is polyphenylene, from which monolithic specimens have also been obtained[29]. Although thermo-oxidative degradation occurs at ~400°C, monolithic polyphenylene is able

to function at far higher temperatures (Fig. 11). Moulded polyphenylene remains effective under a stress of 200 kg cm^{-2} at 300°C. Raising the temperature to 400°C lowers the working stress to 80 kg cm^{-2}, and even at 600°C the stress in monolithic polyphenylene is not completely relaxed to zero: i.e. performance is maintained at this temperature, but only under very small stresses.

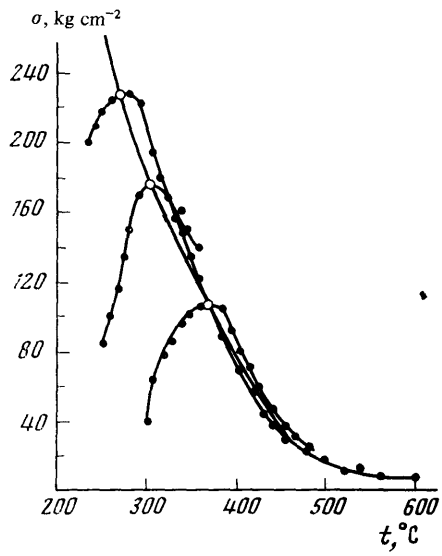


Figure 11. Performance range of polyphenylene.

The extrusion of heat-resistant polymers even at very high temperatures and pressures does not always yield true monoliths, since the extrusion temperature lies below the pour point. Despite this, such caked material is able to function in rigid structures. Thus the aromatic polyester Ekonol 301 is extruded under pressure to yield machinable monolithic material[33]. Articles made of Ekonol retain good mechanical and dielectric properties up to 315°C.

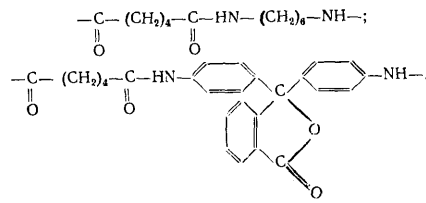
Mechanical properties under hydrostatic pressure have been studied[34] in connection with the problem of obtaining monolithic articles from rigid-chain polyimides at comparatively low temperatures. Under these conditions the polyimide exhibits large plastic deformations and collapses with formation of a neck, so that the polyimide can be processed by cold moulding. The application of hydrostatic pressure to polyimides may tend to raise the limit of forced elasticity and the elongation at rupture, and also to increase Young's modulus[35].

One route for obtaining heat-resistant plastics is the use of oligomers having reactive end-groups[36]. Fibres of a filler (e.g. graphite fibres) are impregnated with solutions of the oligomers and aromatic diamines, and then dried at a high temperature, after which the products are extruded. The resulting plastics possess good mechanical properties.

In the above processing methods the heat-resistant polymers are subjected to high temperatures and pressures, which is often undesirable and may lead to thermal degradation. This can be avoided by producing goods (in particular, films) from solution. In this connection the synthesis of the card type of heat-resistant systems has made a significant contribution to polymer science[37-41]. Such systems contain bulky side-rings, often possessing appreciable polarity, with one of the cyclic elements forming part of the main polymer chain. Thus without loss of heat resistance the polymer acquires good solubility in many readily available organic solvents, so that strong transparent films, whose properties will be described below, can be obtained. Enhancement of solubility can be achieved by the synthesis of "spiral-staircase" polymers containing ladderlike fragments[42].

The production of polymeric goods directly from monomers is currently a leading line of advance in polymer processing. The accompanying polymerisation or polycondensation results ultimately in formation of a finished article. This is sometimes the only possible method for heat-resistant systems, since many heat-resistant polymers do not possess fluidity. Morgan et al[43-45] have shown that it is entirely possible to process the monomers of pyrrones to give articles possessing adequate strength, elasticity, and several other valuable properties. Equimolecular mixtures of the monomers are compressed in a mould at temperatures up to 450°C for 1 h. In this way pyrrones have been obtained from pyromellitic dianhydride, benzophenone-3,3',4,4'-tetracarboxylic acid and biphenyl-3,3',4,4'-tetra-amine, etc. The optimum temperature, pressure, and time can be chosen to give specimens of maximum density, which in this case possess the greatest strength (up to 1475 kg cm^{-2}).

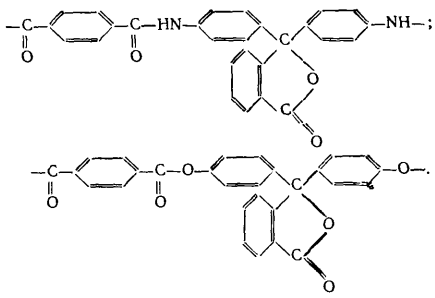
In assessing the effect of the chemical structure of heat-resistant polymers on their properties it must be borne in mind that a change in chemical structure quite often leads to a change in the state of aggregation (e.g. crystallisation), with significant changes in all the properties. The phase must therefore be taken into account. In order to examine the effect of chemical structure and state of aggregation on the mechanical properties of several polyesters and polyamides we shall compare the performance ranges of a few pairs of such polymers[46]. In the first pair of polyamides



the polymethylene segment in the amine component is replaced by an anilinephthalein residue. The performance regions of these polymers (Fig. 12) show that, although their softening temperatures are about the same, the polyamide based on an aromatic diamine withstands far greater stresses at all lower temperatures. Whereas polyhexamethylenadipamide is crystalline, while polyanilinephthaleinadipamide is amorphous, the latter forms a far more rigid monolith, capable of withstanding considerable mechanical loadings.

Comparison of the mechanical properties of an aromatic polyamide and an aromatic polyester in which the diol

residue has the same chemical structure as the diamine residue



permits assessment of the contributions by ester, peptide, and intermolecular (hydrogen) bonds in establishing the set of mechanical properties of the polymer over a wide temperature range. Fig. 13 shows that the curves bounding the performance regions of polyamides lie at considerably higher temperatures than the corresponding curves for polyarenecarboxylates. The largest displacement is found with polymers of aliphatic dicarboxylic acids, since hydrogen bonds continue to "function" at low temperatures, and undergo appreciable cleavage at high temperatures.

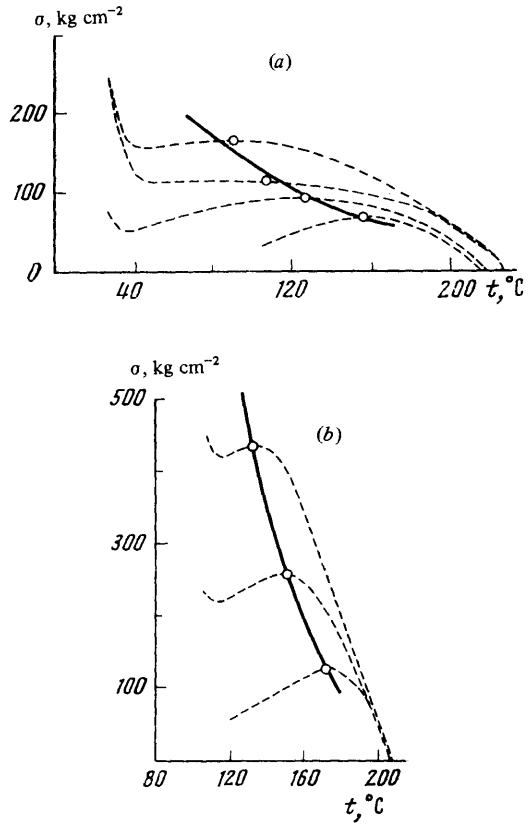


Figure 12. Performance ranges of: *a*) polyhexamethylenadipamide; *b*) polyamide of adipic acid and anilinephthalein.

A clearer idea of the effects both of chemical structure and of intermolecular interaction on the mechanical properties of such polymers can be obtained from the curves bounding the performance regions of polysebacamides and the corresponding polysebacates (Fig. 14). The polyamide formed by sebacic acid and anilinephthalein possesses the largest performance region. The bounding curve undergoes only a slight displacement to lower temperatures on passing to the analogous polyester, but a completely aliphatic polyester based on sebacic acid exhibits a sharp decrease in the mechanical stress limits. Thus the presence of intermolecular (hydrogen) bonds with a repeating unit of almost identical structure shifts the boundaries of the performance region only with respect to temperature, but changing the chemical structure (in the presence of hydrogen bonds) produces displacements with respect both to temperature and to stress.

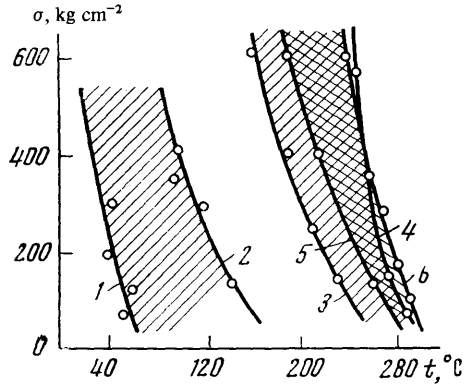


Figure 13. Curves bounding performance regions of various polyamides and polyesters: 1) polyester of sebacic acid and phenolphthalein; 2) polyamide of sebacic acid and anilinephthalein; 3) polyester of isophthalic acid and phenolphthalein; 4) polyamide of isophthalic acid and anilinephthalein; 5) polyester of terephthalic acid and phenolphthalein; 6) polyamide of terephthalic acid and anilinephthalein.

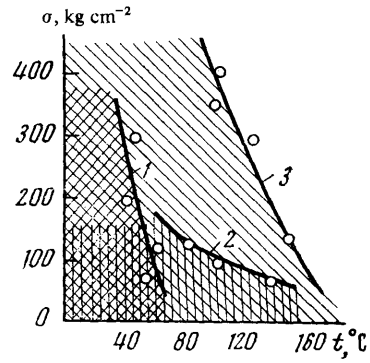
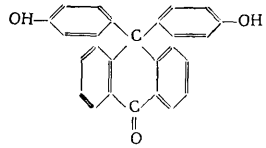


Figure 14. Curves bounding performance regions of polyamides and polyesters based on sebacic acid: 1) polyester with phenolphthalein; 2) polyamide with hexamethylenediamine; 3) polyamide with anilinephthalein.

The difference in softening point between aromatic polyamides and polyesters was used[47] to determine the energy of the hydrogen bonds as 6.6 kcal mole^{-1}. Special attention has been paid[48,49] to the influence of substitution isomerism on the properties of aromatic polyamides[50].

The above systems belong mainly to the group of card polymers containing bulky side-rings. The presence of such rings confers solubility on the polymers, but often prevents their crystallisation, especially if the rings are unsymmetrical. In some cases, however, the presence of a bulky side-ring does not prevent crystallisation, and polyarenecarboxylates based on 9,9-bis-*p*-hydroxyphenylanthrone



are interesting in this respect[51-53]. Like analogous polymers they dissolve readily in many of the usual organic solvents, from which strong, transparent films can be obtained. Such polyesters show a pronounced tendency to crystallise. The structure of poly(hydroxyphenylanthrone terephthalate) and its properties can be changed by varying the conditions of preparation[52]. The use of different methods of polycondensation (at high and low temperatures in solution, interfacial) or different conditions of high-temperature polycondensation (reaction temperatures, rates of heating and cooling of the reaction mass, concentrations of starting materials, nature of the solvent) enabled this polyester to be obtained in crystalline form, in amorphous form, and as a mixture of the two forms‡. The polyester of hydroxyphenylanthrone and terephthalic acid is obtained in the most crystalline form by polycondensation at 220°C in chlorinated biphenyl, 1,2,4-trichlorobenzene, nitrobenzene, and 1-chloronaphthalene. The structure of this polyester can be varied not only by changing the conditions of preparation but also by appropriate treatment—reprecipitation, heating in specially selected solvents—of the finished polymer. The crystallisation of aromatic polyesters based on hydroxyphenylanthrone is accompanied by a deterioration in their solubility.

The presence of an anthrone ring system in a polymer chain favours crystallisation of the aromatic polyesters, and thereby provides further opportunities for improving their heat resistance, and perhaps that of other classes of rigid-chain polymers. Examination of a monolithic, partly crystalline polyester of hydroxyphenylanthrone and terephthalic acid showed a peculiar influence of order on heat resistance. Determination of the performance region of this polyester showed[52] that relaxation processes accelerate sharply, i.e. the material begins to soften, at the same temperatures with a partly crystalline specimen as with the amorphous material (Fig. 15), which suggests that softening involves the amorphous part of the polymer.

‡In the discussion of structure formation in polymers the terms "crystallinity", "crystalline and amorphous parts", etc. must be employed with some caution, especially when applied to aromatic polymers having bulky side-chains. In such case it is better to speak of the ordering of the system, since polyesters of this type cannot be obtained in the usual crystalline form. However, we shall not enter into questions of terminology here, but use these terms with this reservation.

However, the maximum temperature limits of performance become much higher with weakly stressed, partly ordered specimens.

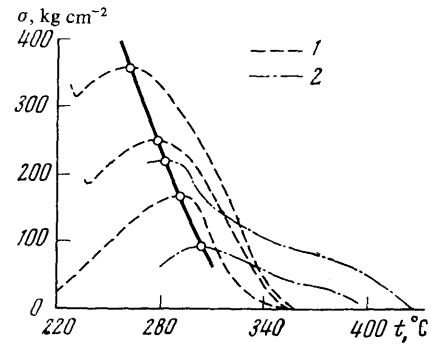
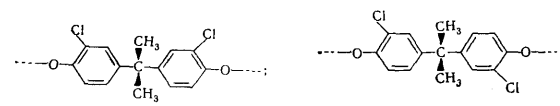


Figure 15. Performance ranges of monolithic specimens of polyester formed by hydroxyphenylanthrone and terephthalic acid: 1) amorphous specimen; 2) partly crystalline specimen.

Interesting results have been obtained[54,55] for the mechanical properties of aromatic polyesters of 3′,3″-dichloro-2,2-diphenylpropane-4′,4″-diol prepared by acceptor-catalysed polycondensation. The chlorine-35 nuclear quadrupole resonance spectra of such systems are characterised by comparatively narrow signals belonging to different crystallographic forms. The reason may be that the chlorine atoms in the diol permit in principle the existence of two rotational isomers.



whose presence in the polyester chain may lead to two isomeric types of macromolecules. Polyesters of this diol and terephthalic acid obtained under various conditions of acceptor-catalysed polycondensation (different reaction media, temperatures, etc.) exhibit several abnormalities of mechanical behaviour. The thermomechanical investigation of films reveal a transition, apparent in a rapid development of deformation at temperatures below the softening range and in the establishment of a plateau (Fig. 16). It was found that the increase in deformation was not due to the usual transition to a state of rubberlike elasticity.

Another interesting abnormality is evident in the determination of performance regions for monolithic specimens of such polyesters. The non-isothermal stress-relaxation curve under conditions of uniaxial compression passes not just through one maximum (as is usual) but through two maxima, which appear in the temperature range of the first increase in deformation on thermomechanical curves obtained at the corresponding stress. Detailed analysis of this phenomenon, based on nuclear quadrupole resonance and on the measurement of heat capacity, suggests[55] that all these anomalies may be due to a transition between

rotational isomers in the residue of the diol, with a consequent conversion of one isomeric form of macromolecule into the other. This transition is activated by mechanical stresses, since increase in stress lowers the transition temperature (Fig. 16).

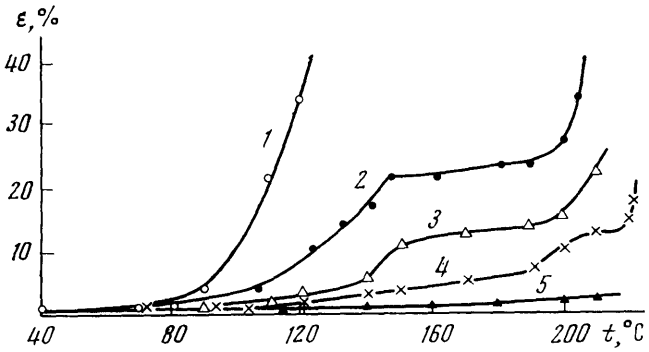


Figure 16. Thermomechanical curves obtained for polyester of 2,2-di-*m*-chlorophenylpropane-*pp'*-diol and terephthalic acid determined at constant tensile stresses (kg cm^{-2}): 1) 200; 2) 100; 3) 50; 4) 25; 5) 100 (repeat test).

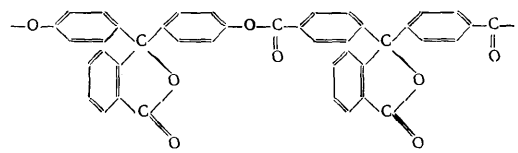
It appeared from the above considerations that the rotational isomers of aromatic polyesters of the dichlorodiphenylpropanediol were quite stable. This opens up the theoretical possibility of synthesising stereoregular polycondensed systems simply by varying the conditions. It also becomes obvious that the structure and properties of rigid-chain polymers can be most efficiently varied during synthesis, since the resulting macromolecular conformations are "frozen", remaining stable on subsequent treatment of the polymer[54,55]. Strength and deformation characteristics were published[56-58] for aromatic polyester films prepared in various media.

Strength cannot be fully assessed from the breaking stress, which merely provides a comparison of the strength properties of polymers differing in chemical structure. To obtain a more complete measure of the strength properties of polymers we must determine the parameters in Zhurkov's durability equation

$$\tau = \tau_0 e^{\frac{U_0 - \gamma\sigma}{RT}}, \qquad (6)$$

where τ_0 is the pre-exponential factor, U_0 the initial activation energy of fracture, γ a structure-sensitive parameter, and σ the constant stress. Numerical values of U_0 and γ were determined[17,59] by a modified thermomechanical method and by the application of Bailey's criterion to tests with uniaxial stretching at various temperatures. The initial activation energy of fracture was found to be low (U_0 = 30 kcal mole^{-1}) for globular polyesters of phenolphthalein with isophthalic and terephthalic acids. This indicates that the bonds between the globules forming a film or a monolithic body are fairly weak. The type of supermolecular structure of such systems has an appreciable influence also on the relaxation processes accompanying deformations remote from fracture. Greater rigidity at comparatively low temperatures and larger equilibrium stresses are obtained with a globular than with a fibrous structure. With rise in temperature the opposite situation is found, for the ease of rupture of the weak bonds between globules leads to premature breakdown of the material. Globular material is more homogeneous in structure, which results, in particular, in well defined temperature dependence of the relaxation parameters[60].

The effect of bulky side-rings in conferring solubility is confirmed by the synthesis of soluble, extremely heat-resistant polyesters of 4,4-diphenylphthalide-*pp'*-dicarboxylic acid with various diols (resorcinol, quinol, biphenyl-*pp'*-diol, etc.)[61]. Among them the polyester of this acid with phenolphthalein



is especially interesting, its performance range surpassing those of other aromatic polyesters with respect both to temperature and to stress at a given temperature. Thus the introduction of an additional bulky, polar ring not only improves the solubility but also extends the ranges of stresses and temperatures over which the polymer remains solid and able to function in rigid structures.

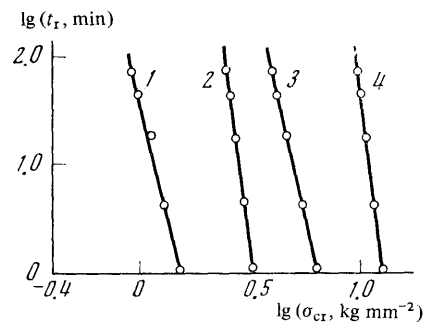
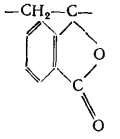


Figure 17. Dependence of lg t_r on lg σ_{cr} at 20°C for the polymers: 1) polyethylene glycol (M = 20 000); 2) poly(ethylene glycol sebacate); 3) polyester of sebacic acid and phenolphthalein; 4) polyester of terephthalic acid and phenolphthalein.

In concluding our account of the structure and properties of polyesters we must pay special attention to their relaxation properties, which largely determine the heat resistance. Measurement of these properties over a wide temperature range has enabled[62] the effect of chemical structure on heat resistance to be studied for a series of polyesters. Comparison of the relaxation parameters of the sequence from aliphatic polyethers to polyesters containing different numbers of aromatic rings in the repeating unit shows that, under otherwise similar conditions, an aromatic polyester (polyarylate F-2) retains the relaxing stress for a far longer period than any other polymer in this sequence (Fig. 17). As we pass

from polyethers to polyesters and as the latter become saturated with benzene rings the above relations shift regularly to greater critical stresses. Thus extension not only of the temperature ranges of mechanical performance but also of the range of working stresses themselves can in practice be achieved by controlled variation of the chemical structure of the polymer to increase the relative proportion of aromatic rings in the repeating unit.

Special importance must be attached to the presence of bulky (polar) groups, whose beneficial effect on solubility and heat resistance when in the side-chain is especially clearly demonstrated with cardlike carbon-chain polymers, an example of which is polymethylenephthalide[63,64]



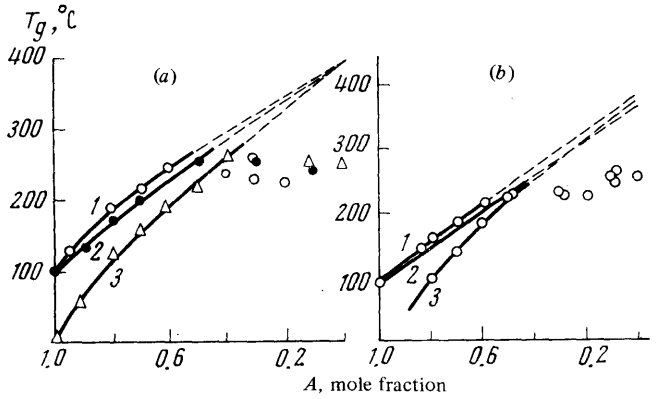


Figure 18. Dependence of glass point determined: *a*) by thermomechanical method; *b*) from performance regions on composition of copolymers [of methylenephthalide] with (*A*, mole fraction): 1) styrene; 2) methyl methacrylate; 3) methyl acrylate.

This polymer can usefully be regarded as a substituted polyethylene possessing incomparably greater heat resistance than either polyethylene itself or its other derivatives. Thus the glass point of polyethylene is −130°C, and that of polystyrene is 100°C, whereas thermomechanical curves suggest that polymethylenephthalide has a glass point of 300°C. However, this last polymer undergoes intense thermal degradation at these temperatures, so that the true softening temperature may be still higher. Calculation by means of Eqn. (8) gave a softening point of 390°C. Calculated and experimental softening points were tested by examining a series of copolymers with styrene, acrylonitrile, methyl methacrylate, methyl acrylate, and other monomers, which showed[64] a smooth rise to 250°C with increase in the methylenephthalide content (Fig. 18). Further increase produced no further rise in softening point of the copolymer, which remained constant in the range 220–250°C. The observed constancy of the softening temperature with variation in the composition of a copolymer is evidently due to thermal degradation at this temperature. The softening point of polymethylenephthalide itself can be determined only by extrapolating the composition dependence of the glass point of the copolymers to zero concentration *c* of the second comonomer, which yields a glass point lying in the range 370–380°C, in good agreement with the calculated temperature.

Thus the presence of card groups in a carbon-chain polymer leads to a sharp increase in heat resistance, as in heterochain polymers. In such systems the heat resistance exceeds the thermal stability, and the latter thus limits their performance. This has extremely important practical consequences. With a large margin of heat resistance present, the polymer can be modified by copolymerisation, plasticisation, etc. without danger of lowering its actual softening temperature. In particular, the quantity of plasticiser or the concentration of phthalide groups on copolymerisation with other monomers can be varied within wide limits. Nevertheless, the introduction of even a small quantity of phthalide segments into an ordinary carbon-chain polymer leads to a considerable improvement in its heat resistance.

Polyimides currently form one of the most important classes of heat-resistant polymers, since they form the basis of plastics, films, fibres, coatings, and other objects which retain their performance at high temperatures. Aromatic polyimides when heated often pass from a vitreous state directly into a viscous fluid, but in several cases they may develop rubberlike elasticity, as do polymers having flexible macromolecules. A characteristic of heat-resistant systems is that the range of such elasticity is displaced significantly to higher temperatures, which its upper limit determined by the intensity of thermal degradation and cross-linking. Furthermore, the modulus of rubberlike elasticity is substantially greater for heat-resistant systems than for flexible-chain polymers. Polyimides may yield either non-softening rigid polymers or softening polymers having normal Young's moduli of 50–100 kg cm^{-2}, depending on the proportion of flexible units in the polymer chain[65]. The thermomechanical properties of several polyimides were explained[66] by the formation of a labile network, whose presence was especially apparent above 250°C.

Determination of the temperature range of rubberlike elasticity from the thermomechanical curve without further verification of the reversibility of deformation may lead to substantial errors. The presence of a plateau on this curve is a necessary but not a sufficient condition for the development of rubberlike elasticity, since it may be due to thermal degradation and several other secondary processes: verification of the reversibility of deformation in the region of the plateau is therefore absolutely necessary. Fig. 19 shows thermomechanical curves, determined on uniaxially stretched films[31], for polyimides of oxy-*pp'*-dianiline and oxy-4,4'-diphthalic acid (curves *1* and *1'*) and of anilinephthalein and sulphonyl-4,4'-diphthalic acid (curves *2* and *2'*). The broken curves represent the properties of the polymers subjected to a constant stress, whereas the full (primed) curves apply to periodic loading. Fig. 19 shows that part of the deformation in the region of the plateau is reversible (rubberlike elasticity), while part is irreversible (viscous flow). The former polymer (curve *1*) possesses a wide range of rubberlike elasticity (280–500°C). Curve *1'*, determined under a variable load, shows that the modulus of rubberlike elasticity $E = \Delta\sigma/\Delta\epsilon$, where $\Delta\sigma$ is an increment of stress and $\Delta\epsilon$ the

consequent increment of reversible deformation, increases continuously with rise in temperature (from 30 to 100 kg cm^{-2} from 300 to 430°C). The specimen does not exhibit rubberlike elasticity above 460°C, which, like the increase in the modulus, is attributed to chemical cross-linking. A similar modulus (20 kg cm^{-2}) was observed in the transition zone for the second polyimide. The specimen had an extremely high glass point and hence a narrow range of rubberlike elasticity (430–470°C), bounded by the intensity of degradation and cross-linking.

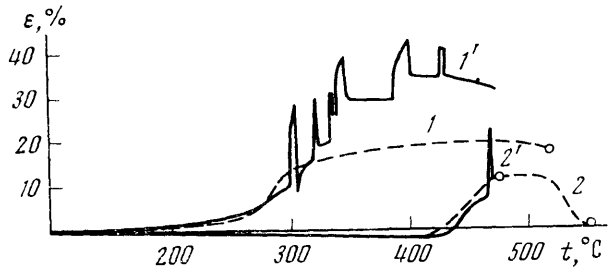


Figure 19. Thermomechanical curves for polyimide films.

Many types of aromatic polyimides are roughly equivalent in thermal stability, from which follows the conclusion of practical importance that the range of the state of rubberlike elasticity can be extended significantly by lowering the glass point either by introducing oxa, carbonyl, etc. groups into the polymer chain or by diminishing the number of fused rings. We again stress that, despite the sharp drop in glass point, the thermal stability remains almost undiminished; thus there is no direct link between the glass point and the temperature at which loss in weight begins. Rubberlike elasticity is exhibited not only by polyimides but also by other heat-resistant polymers, e.g. polybenzoxazoles[67]. The thermal stability of these systems is also little affected by the introduction of oxa, thia, or carbonyl groups into the main chain.

When the thermomechanical properties of these polymers are determined in the presence of small mechanical stresses, the glass points are often close to the decomposition temperatures. The former can conveniently be sought by making thermomechanical tests with comparatively large stresses. This lowers the glass point considerably, but a plateau is still formed on the thermomechanical curve because of the high moduli of rubberlike elasticity, and it is easy to determine both the glass point and the pour point T_{fl}. The true temperatures of these points can be determined by plotting T_g and T_{fl} against stress and extrapolating to zero stress. This procedure enables glass and pour points to be found when they lie above the decomposition temperatures of the polymers.

On the whole the introduction of "hinge" atoms into the repeating units of polybenzoxazoles, polyimides, and other heat-resistant polymers permits control not only of the glass point but also of strength and deformation properties. A suggested classification of polyimides was based[68,69] on the presence and site of hinge bonds. The resulting classes differed in physical properties. A physical model shows[69] that the rearrangement and introduction of "flexible" bonds, allowing for interaction between chains through transverse groups, controls the number of degrees of freedom of such a system. This classification can be applied also to other systems[70,71]. The introduction of various hinge groups—oxa, thia, carbonyl, peptide, carboxylate, etc.—not only enhances the deformability of heat-resistant systems but also facilitates their fabrication into monolithic articles by hot extrusion, injection moulding, etc. to yield polymeric materials having excellent mechanical properties[5]. However, the main advantage of many aromatic polymers—their high heat resistance—is in considerable measure lost.

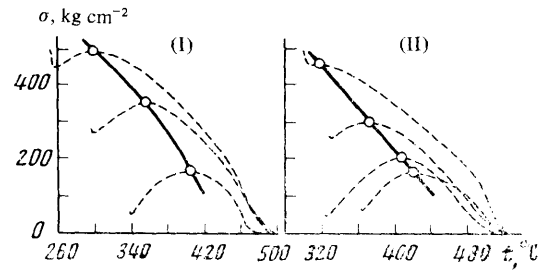
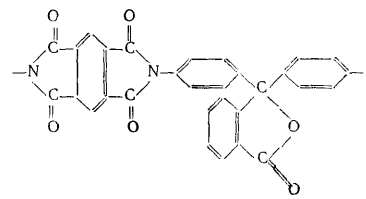
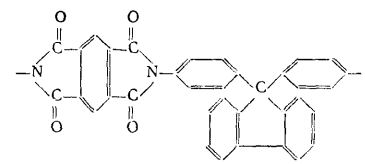


Figure 20. Performance ranges of monolithic specimens of polypyromellitimides (I) and (II).

More detailed consideration of this problem in relation to aromatic polyimides shows that, on introduction of the above groups, the heat resistance of the polymers will differ little from that of aromatic polyesters, aromatic polyamides, and other polyheteroarylenes. The performance ranges of monolithic specimens of the polyimides



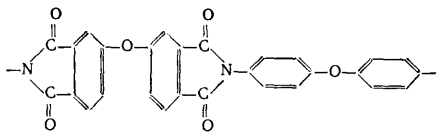
(I)



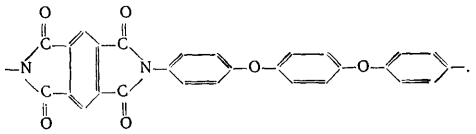
(II)

which do not contain the above groups, are extremely wide with respect both to temperature and to stress (Fig. 20)[32]. Thus at 300°C these plastics can function under a load of 500 kg cm^{-2} for a short time, and at 400°C they withstand 200 kg cm^{-2} (most structural plastics are completely devoid of performance at this temperature, owing both to degradation and to softening or flow). The maximum performance limits for the polyimides (I) and (II) are respectively 490 and 515°C. To compare the performance of these polyimides with that of polyimides containing "hinge" groups and also of several traditional polymers, we plot on the same diagram (Fig. 21) the curves bounding the performance regions of these systems.

The heat resistance of the polymeric materials increases significantly as the main polymer chain becomes saturated with aromatic rings and with other heterocycles. Some of the solid polyimides represented on Fig. 21 are not true monoliths (Nos. 9–11), and their performance ranges might be extended further if true consolidation of the material were achieved. The heat resistance can be improved also by crystallisation. Not only the number but also the relative arrangement of rings is no less important for the heat resistance of polyimides and other systems [31,32,72]. With identical numbers of imide rings, benzene nuclei, and all other groups and elements, the heat resistance is enhanced by a greater degree of ring fusion. Thus the polyimide



is considerably less heat-resistant than is



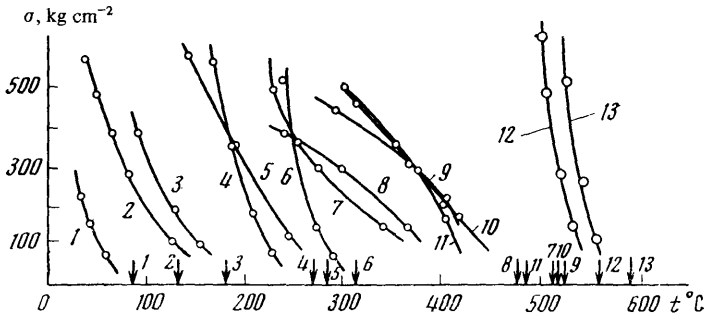


Figure 21. Curves bounding the performance regions of representatives of various polymer series: 1) poly(methyl methacrylate); 2) poly(2,2-diphenylpropane-*pp'*-diol carbonate); 3) poly(propane-2,2-di-*p*-phenylene isophthalate); 4) poly(phenolphthalein isophthalate); 5) polyimide of oxy-*pp'*-dianiline and oxy-4,4'-diphthalic acid; 6) polyamide of isophthalic acid and anilinephthalein; 7) polypyromellitimide of oxy-*pp'*-dianiline (amorphous); 8) polypyromellitimide of *p*-diphenoxybenzene-*p'p''*-diamine; 9) polypyromellitimide of oxy-*pp'*-dianiline (partly crystalline); 10) polypyromellitimide of 9,9-diphenylfluorene-*p'p''*-diamine; 11) polypyromellitimide of 3,3-diphenylphthalide-*p'p''*-diamine; 12) sodium silicate glass; 13) potassium silicate glass. The arrows indicate the softening points of the polymers. Specimens 5, 7, and 8 were obtained by formation from a preliminary polymer (polyamino-acid).

In conclusion we again direct attention to the possibility of obtaining extraordinarily heat-resistant organic polymers (polyimides). In this respect they approach quite closely to inorganic glasses, which many authors [73] now regard as polymeric in structure. Fig. 21 includes curves bounding the performance regions of two inorganic glasses, which are displaced to higher temperatures than the corresponding curves for polyimides based on anilinefluorene and on anilinephthalein, but not so greatly. In the preparation of polymers capable of functioning at high temperatures it must be borne in mind that the upper temperature limit of their performance may be governed not by loss of heat resistance (softening) but by the beginning of intense thermal degradation, i.e. loss of thermal stability. In several cases, therefore, it may be important to determine the thermal stability rather than the heat resistance.

Considering in greater detail the relaxation properties[30] of block specimens of one of the most important aromatic polyimides—the polypyromellitimide of oxy-*pp'*-dianiline—we note that the properties of its films have been studied in some detail[6], but different views are held on several of its principal physical properties. Results for the glass point are especially contradictory, for temperatures of 250, 380, and >500°C have been found [6,66,74]. The temperature dependence of the parameter α in Eqn. (1) for block specimens of this polymer shows (Fig. 22) two relaxation transitions (at 270 and 400°C), which may be due to devitrification. Extrapolation to $\alpha = 0$ yields [12] $T_g = 520$–530°C. However, this polymer exhibits a tendency to crystallise, which may be responsible for the break in the temperature dependence near 400°C.

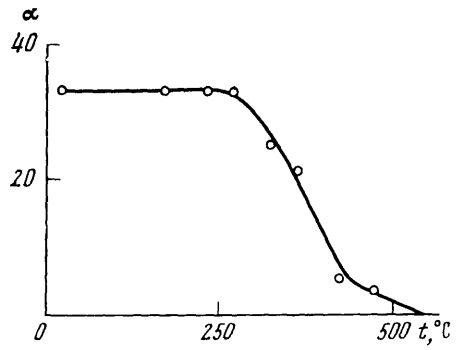


Figure 22. Temperature dependence of α for block specimens of the polypyromellitimide of oxy-*pp'*-dianiline.

The temperature dependence of $\sigma_{\infty, cr}$ exhibits a similar pattern: Fig. 23 shows that this critical equilibrium stress remains approximately constant over a wide temperature range, after which it decreases smoothly with rise in temperature. The curve bounds the region of stresses and temperatures in which the solid polymeric material can function under conditions of stress relaxation for a long time. With the above polypyromellitimide this region is quite large with respect both to temperature and to stress, although polyimides having a card structure are able to operate under far larger stresses at the same temperatures (cf. Figs. 23 and 20).

Investigation of the effect of chemical structure on the properties of polyimides must take into account their possible tendency to crystallise. This tendency varies in complicated fashion with the rigidity of the chain [75–77],

which is determined by the presence of aromatic nuclei: increase in the content of such rings initially prevents crystallisation, and at a certain content the tendency to crystallise becomes minimal; but after this the strengthening of intermolecular interaction intensifies the tendency, leading to an infusible polymer. The crystallisability is significantly affected by the position of the aromatic ring in the chain and by the presence of a solvent [75,76].

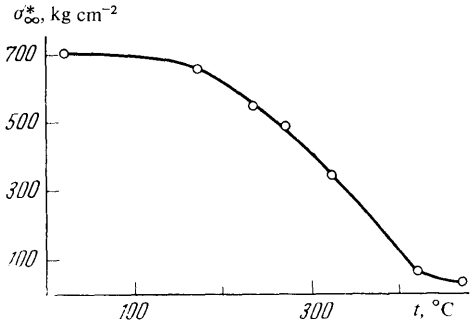


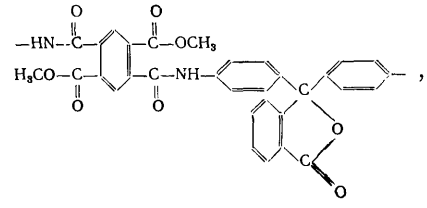
Figure 23. Temperature dependence of $\sigma^*_{\infty,cr}$ for block specimens of the polypyromellitimide of oxy-*pp'*-dianiline.

Close attention has recently been paid to the hydrolytic stability of polyimide films. Keeping such a film in water produces a rapid fall in tensile strength and in elongation at break. This phenomenon is characteristic both of polyalkyl-imides (based on pyromellitic dianhydride) and of completely aromatic systems. With the former the elongation at break falls rapidly from 200 to 100–40% after immersion in water at 70–100°C for 50–100 h. [78] A film of poly(oxy-*pp'*-dianiline pyromellitimide) [79] exhibits the same peculiarities, although the quantity of water absorbed is about 4%, compared with 0.4% for polyalkyl-imides.

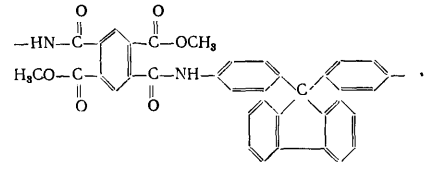
It is possible [80] to restore the strength and deformation properties of Kapton polyimide film after they have been sharply reduced by hydrolysis in distilled water at 100°C. The tensile strength of 1860 kg cm^{-2} and elongation of 62% of the initial film had fallen to 1050 kg cm^{-2} and 6.3% after standing in water at 100°C for 12 days. Heat-treatment of the hydrolysed film at 224–310°C for a few hours increases the tensile strength to 1700–1800 kg cm^{-2} and the corresponding elongation to 38–51%. Thus the amino-acid units formed by hydrolysis are recyclised, rapidly in the early stages and slowly in the later stages; this occurs not only in the solid state [81,82] but also in solution [83].

In this connection it is very important, in the two-stage formation of polyimides and other polymers, that cyclisation of the initial polymer should be as complete as possible. The presence of uncyclised units not only diminishes the heat resistance but also sharply decreases the hydrolytic stability and impairs several other properties. It is thus very important to determine the optimum conditions for cyclisation. It was shown in the case of poly(3,3-diphenylphthalide-*pp'*-dicarboxylic hydrazide) that its cyclisation to polyoxadiazole takes place rapidly at temperatures below the glass point of the polyhydrazide [84,85]. Chemical cyclisation is accompanied here by considerable contraction of the repeating unit. Passage through the glass point makes possible, of course, full development of the mobility of the polymer chain, as a result of which the intramolecular cyclisation is considerably accelerated.

In other cases cyclisation is rapid even in the vitreous, solid state, as has been shown for the polyimides resulting from cyclisation of the alkoxycarbonylated polyamides



(III)



(IV)

Detailed examination has shown [86] that, although the glass point of (IV) is 290–300°C, the polymer has undergone intense cyclisation over the range 150–250°C. With certain other polyimides rapid cyclisation takes place above the glass point of their polyamino-acids [87,88]. However, these workers themselves [87,88] admit that the polyamino-acid contained a large quantity of solvent (*NN*-dimethylformamide), which not only lowered the glass point of the system but also changed the whole kinetics of cyclisation. Calculations based on Eqn. (8) gave glass points of these acids considerably higher than the published temperatures [87,88].

Thus heat-resistant aromatic systems can undergo rapid and extensive cyclisation in the solid phase either above the glass point of the initial polymer or in the vitreous state. Both the rate and the extent of cyclisation are determined, not by the physical state of the system (vitreous or rubberlike elastic), but mainly by the chemical structure, which governs the kinetics of the process and the need for a particular contraction of the repeating unit on formation of an intramolecular ring.

The properties of heat-resistant polymer films can be modified by synthesising mixed systems, which often tend to change the structure and improve the mechanical properties of the films. The properties of polyheteroarylenes can be modified by preparing polyamide-imides, whose solutions are more stable (in contrast to solutions of polyamino-acids); stable films can be obtained from them without heat-treatment [89]. The preparation and properties of polyamide-imides and polyester-imides of ordered structure have been described [90–93]. The latter polymers, because of the introduction of an ester group into the dianhydride component, possess several specific properties and characteristics of their state of aggregation. The macromolecules show well defined spontaneous orientation as a consequence of a conformational transition into a more ordered state, occurring in the region of the glass point of the polymer (210–230°C), where the molecular units become sufficiently mobile. The transition is accompanied by the appearance in unoriented films of an axial (in some cases axial-planar) texture with its axis perpendicular to the surface of the film. Polyester-imides undergo extensive crystallisation when heated to

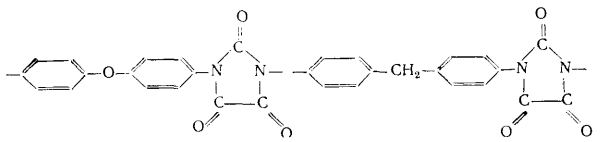
350–380°C. Drawing these polymers at temperatures near the glass point yields a typical amorphous texture, which, together with the spontaneous orientation effect, indicates that considerable order is present in the amorphous state. Further heating enables highly crystalline structures to be obtained, which are stable up to 420–450°C. X-Ray diffraction showed that increasing the number of phenyl rings in the diamide component merely increased the parameter c of the unit cell, without affecting the relative arrangement of the macrochains. The characteristic behaviour of polyesterimides is explained by enhanced rigidity of the macromolecules and interaction between phenyl rings, leading to a non-spherulitic type of crystallisation[91–93]. Films of polyimides and polyamidoimides are able to withstand ultraviolet radiation[94].

Other mixed heat-resistant systems of interest are polyamidoquinoxalines[95] and polybenzoxazolimides, whose mechanical properties have been reported in detail[96]. The tensile strength of films of these polymers lies in the range 1600–2200 kg cm^{-2}, and the elongation at rupture between 5% and 40%. The mechanical properties of films are significantly affected by the solvent in which the polymer had been dissolved. Evaporation of different solvents will yield films possessing appreciably different properties, probably because of differences in structure formation.

The properties of aromatic polymers, including polyimides, can be modified by the introduction of perfluoroalkylene segments[97,98], which is a more efficient method of lowering the glass point than is the introduction of ether links. The glass point can be varied within quite wide limits by changing the length of the perfluoroalkylene chain. Films, monolithic articles, and fibres possessing satisfactory mechanical properties have been obtained from modified polyimides. The glass point can be raised also by the introduction of card groups[10,99], their effect being most marked in an aliphatic chain (e.g. in aliphatic polyesters). Introduction of a card group, of course, increases both the skeletal rigidity of the chain and its kinetic rigidity, because of the large bulk of the group. Hence the significant rise in the glass point in comparison with the initial polyesters.

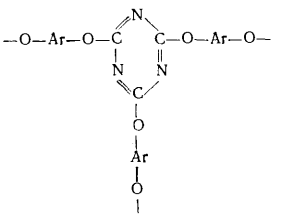
Heat resistance can be improved by cross-linking linear polymers, e.g. polyamidoquinoxalines, containing functional side-groups[100]. The system thereby loses its fluidity, and when filled possesses enhanced strength, which is maintained at very high temperatures. The strength of heat-resistant polymers can be increased by drawing and heat-treating them in a swollen state. Application of this procedure to poly-*m*-phenylenisophthalamide leads to significant increases in Young's modulus, tensile strength, and (with moderate degrees of drawing) elongation at break[101]. A very appreciable improvement in mechanical properties can be achieved by choosing optimum drawing conditions (type of solvent, temperature, duration of drawing, etc.).

A recent paper[102] has described the preparation and properties of polyparabanic acids



which possess high glass points (290–300°C), are readily processed into monolithic articles by stamping or extrusion, and form very strong films possessing good dielectric properties preserved at high temperatures.

An interesting investigation on the preparation and properties of heat-resistant aromatic polymers has been concerned[103,104] with polycyanates, obtained by the polycyclotrimerisation in mass of dicyanates of various aromatic diols. This reaction produces a network



of high regularity resulting from the enhanced selectivity of cyclotrimerisation of O–C≡N groups[103,104]. Polycyclotrimerisation is characterised also by a high conversion of such groups, reaching 98–99%. All these features lead to the formation of systems having a very dense network and possessing increased resistance to mechanical impacts and several other interesting properties[105]. The network systems exhibit not only increased resilience but also appreciable signs of structural order, with almost constant packing coefficients of the macromolecules in the networks close to the mean value (k = 0.681) for amorphous monolithic polymers[15]. Thus three-dimensionally cross-linked aromatic polymers are similarly ordered systems to amorphous and slightly crystallised linear polymers. The heat resistance of such networks is limited by the temperature at which their degradation begins; for many of them the limit is 300–350°C.

Not only monolithic articles and films but also fibres retaining their performance at high temperatures can be obtained from heat-resistant aromatic polymers. Without considering in greater detail this special aspect, we note merely that information has been published on the properties of fibres based on aromatic polyamides and various irregular copolyamides[106] and that fibres have been obtained from alternating polyoxadiazolimides[107], polyamide–hydrazides[108–113], and adamantane[114] and other polymers[115,116], among which considerable interest attaches to poly-2,2′-octamethylene-5,5′-dibenzimidazole, obtained by interaction between biphenyl-3,3′,4,4′-tetraamine and derivatives of sebacic acid. This last polymer forms stable films and fibres, whose crystalline state is affected significantly by the solvent[116]. In particular, replacing the solvent (formic acid by acetic acid) changes the parameters of the unit cell. Experimental results obtained by X-ray diffraction, thermography, and infrared spectroscopy combine to indicate the formation of a crystalline solvate state, which considerably alters the physical properties of this polymer.

IV. RELAXATION TRANSITIONS

Relaxation transitions in polymers are usually detected from the temperature dependence of the tangent of the angle for mechanical and dielectric losses tan δ. Heat-resistant polymers are extremely interesting to investigate, since they exist in the vitreous or crystalline state over a wide range of temperatures, within which many transitions can be discovered. Study of the temperature dependence of tan δ is not only of scientific value for identifying relaxation transitions but also of considerable practical value as a method of quality control of the article

during processing. A still more complete picture is obtained by combining this method with differential thermal analysis. An instrument has been described[117] for the simultaneous determination of dielectric constant and losses, together with differential thermal analysis.

The appearance of particular relaxation transitions will depend on the previous thermal history of the specimens, their crystallinity, and other factors, as well as the method of investigation. It is interesting to trace the transitions in poly-(2,6-diphenyl-1,4-phenylene ether)[118], amorphous specimens of which exhibit a distinct maximum in the temperature dependence of E'' at ~230°C, which corresponds to the glass point. A slight maximum is observed at lower temperatures (~130°C), whose appearance is due to twisting vibrations of the phenylene groups. This transition is more clearly evident in the dilatometric curve, which shows a break near 120°C as the coefficient of cubical expansion increases. The temperature dependence of tan δ for dielectric losses reveals new transitions at 290, 340, and 485°C.

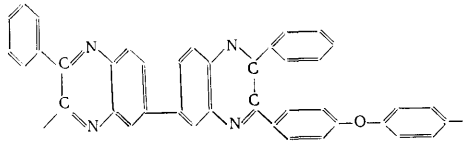
The influence of the previous thermal history on dynamic and static mechanical properties has been studied in detail on polyimides obtained by the cyclisation of polyamino-acids[119]. The temperature dependence of tan δ and that of Young's modulus vary with the rate of heating and the temperature at which cyclisation occurred. The presence of uncyclised units and the possibility of chemical cross-linking at very high temperatures lead to "post-cyclisation" over a certain temperature range during testing, with the appearance of additional peaks in the temperature dependence of tan δ. This applies also to the effect of water and of residual solvent, an aspect which must be discussed in greater detail.

Whether low-temperature transitions in polyimides are due to the molecular nature of the repeating units or to the presence of impurities (e.g. water) has been a matter of debate. A special investigation[120] has revealed three distinct maxima below 130°C in the temperature dependence of tan δ for polyoxy-*pp'*-diphenylenepyromellitimide containing no water: the first, γ-transition occurs at −123°C; the second, at 77°C, is attributed to β°-relaxation; and the third, very weak maximum at −27°C is due to residual moisture in the specimen. Even a small quantity of water (0.225%) changes the picture significantly: a blurred peak is observed from −123 to +77°C, probably owing to the superposition of all the above relaxation processes. Detailed analysis[120] of the temperature dependence of tan δ for samples with different water contents has shown that the transition at −27°C is actually due to the presence of water in the polyimide.

Serious attention must therefore be paid to the importance of removing solvent residues in the investigation of the dynamic mechanical properties of heat-resistant polymers, since its presence may not only distort the temperature dependence of tan δ but also lead to chemical changes at high temperatures. Hence special methods have been developed[121] for examining dynamic mechanical properties, involving attempts at the complete removal of residual solvent. The product of the polycondensation of napthalene-1,4,5,8-tetracarboxylic acid with biphenyl-3,3',4,4'-tetra-amine underwent irreversible chemical changes involving the formation of chemical cross-links, "postcyclisation", etc. even after complete removal of residual solvent[121]. However, the low-temperature peak of tan δ (at −100°C) remained in all cases, so that these irreversible changes do not suppress the mobility of the kinetic units apparent at low temperatures.

The use of dynamic methods to investigate relaxation transitions yields conclusions in several cases as to the mechanism of the relaxation processes accompanying orientation, shrinkage, etc. Thus three temperature regions are found in which a Kapton film shrinks at a maximum rate[122]: the first maximum is observed near 90°C whatever the degree of preliminary drawing at room temperature; a second maximum appears in the region of 200°C only with films that have been stretched by 25%; and the third maximum near 350°C applies to films that are 40% oriented. Each of these maxima occurs roughly at the temperatures of maxima in tan δ for mechanical and electrical losses. Hence the rapid shrinkage after these temperatures have been reached is due to an increase in the molecular mobility of the polyimide macromolecules. Thus a comparative investigation of the temperature dependence of tan δ and of other (static) characteristics—Young's modulus, rate of shrinkage, etc.—may provide valuable information on the establishment of the set of mechanical properties or of polyimides, which has been made for aliphatic and aromatic polyimides[123].

A fundamental investigation of transitions in heat-resistant aromatic polymers was made[124] on a long series of amorphous polyquinoxalines, among which that having the structure



was examined in greatest detail by a variety of methods. Polymers of this type can occur in three isomeric forms, which was regarded[124] as preventing their crystallisation. A single sharp maximum is observed in the temperature dependence of tan δ, E'' and ϵ'', corresponding to vitrification of the polyquinoxalines, the maximum in the dielectric measurements being displaced several tens of degrees to higher temperatures. A weak, additional peak near 210°C is attributed to impurities; in any case, it cannot be explained by the thawing out of the motion of phenyl groups, since it appears even in their absence. The temperature dependence of the heat capacity also showed a transition (vitrification), which was confirmed by dilatometric measurements. Analysis of experimental results obtained by various methods suggested that the appearance of mobility in polyquinoxalines was due not to torsional vibrations but to deformation of the polymer chain itself, which had the form of a tape. The flexibility of such a tape depends on the presence of particular heteroatoms in the main chain.

The most significant transition in a heat-resistant polymer is that involving softening or vitrification. It is therefore extremely important to be able to calculate the glass point T_g solely from the chemical structure of the repeating unit. It was suggested initially[125] that use could be made of the relation

$$\lg T_g = \frac{d}{M}\sum_i K_i' + A', \qquad (7)$$

in which d is the density of the polymer, M the molecular weight of the repeating unit, $\Sigma K_i'$ is its effective volume, comprising the effective volumes of the atoms and groups of atoms forming the unit, and A' is a parameter representing a given series of polymers. This equation holds

well for several series (aromatic polyesters and polyamides, polymethacrylates), Numerical values of K_i' and A' can be found from the original paper [125].

Table 1. Increments K_i^* for various atoms and types of intermolecular interaction.

Atom or interaction	Conventional symbol	Value
Carbon	K_C^*	10.739
Oxygen in side-group	$K_{O,s}^*$	3.925
Oxygen in main chain	$K_{O,m}^*$	−5.244
Hydrogen	K_H^*	−1.248
Nitrogen in side-group	$K_{N,s}^*$	9.520
Nitrogen in main chain	$K_{N,m}^*$	2.185
Chlorine	K_{Cl}^*	7.242
Silicon	K_{Si}^*	19.570
Hydrogen bond	K_h^*	7.333
Dipole-dipole*	K_d^*	7.333
Symmetry coefficient**	K_p^*	10.500

*The coefficient K_d^* is introduced in all cases in which a hydrogen atom is replaced by any type of radical other than phenyl. This rule does not extend to polyisoprene and polychloroprene. When two hydrogen atoms are replaced by identical radicals, the value 0.5 K_d^* is introduced.
**The coefficient K_p^* is introduced if all the aromatic rings in the main chain are substituted in the *para*-position.

Later a general scheme of calculation was proposed [126], applicable to polymers of any series. The glass point was determined from the relation

$$\lg T_g = \frac{\sum_i K_i^*}{N_A \sum_i \Delta V_i} + A, \qquad (8)$$

where $\sum_i K_i^*$ is an additive quantity having the dimensions of a volume and connected with the packing coefficient k and the coefficient α_G of cubical expansion, $\sum_i \Delta V_i$ is the van der Waals volume of the repeating unit, comprising the volumes ΔV_i of all the component atoms, $A = 1.435$ is a parameter of linear polymers of any chemical structure, and N_A is Avogadro's number. The quantities K_i^* occurring in ΣK_i^* are characteristic of each element and each type of intermolecular interaction, and are listed in Table 1. With their values known, it is easy to calculate the glass point of a polymer by means of Eqn. (8) provided that its chemical structure is known. It is first necessary to find [15,127] the van der Waals volume of the repeating unit. Calculated and experimental glass points show good agreement [126] for many polymers of the most diverse structure. Fig. 24, in which the theoretical dependence of the glass point on $\sum_i K_i^*/N_A \sum_i \Delta V_i$ has been drawn, and experimental values have been plotted, confirms that formula (8) holds over a very wide temperature range.

It is thus theoretically possible to calculate the glass point of a polymer before it has been synthesised: the applicability of Eqn. (8) has been subjected to the most detailed verification on heat-resistant polymers. Use of the above scheme of calculation to predict glass points with the aim of synthesising polymers having specified properties has been applied [128] to heat-resistant systems containing fluorine. Other problems can also be solved by this means. Thus, knowing the increment K_d^* representing the effect of intermolecular interaction on the glass point, we can determine from Eqn. (8) the number of chemical groups in the repeating unit that are able to interact in this way and how many are excluded from interaction by steric hindrance. With aromatic polyimides, for example, only two of the four possible carbonyl groups enter into interaction. It is noteworthy also that carbonyl groups enclosed directly between aromatic ring systems are also incapable of intermolecular interaction because of steric hindrance, as has been demonstrated by an independent method [129].

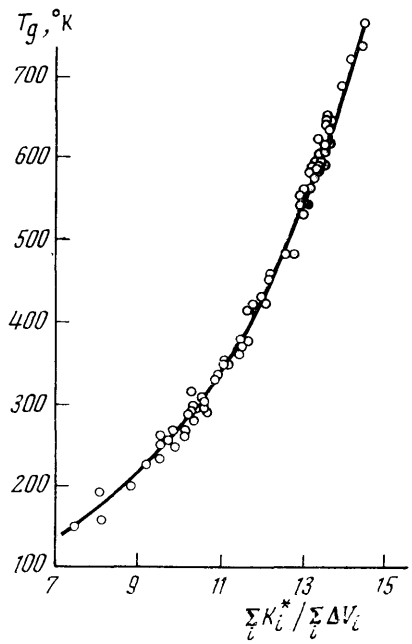
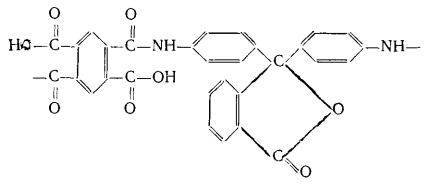
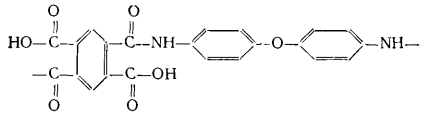
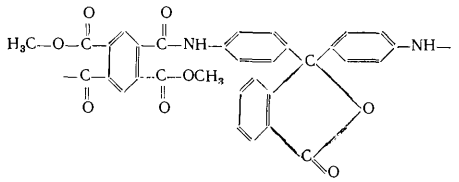
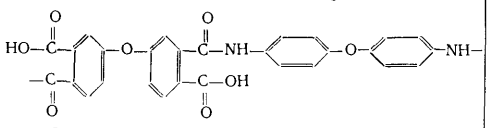
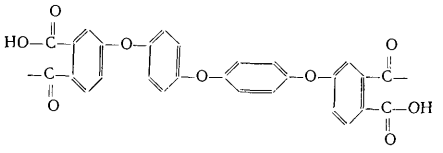
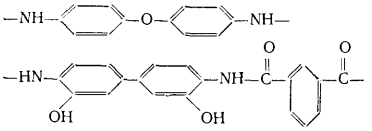
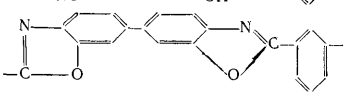
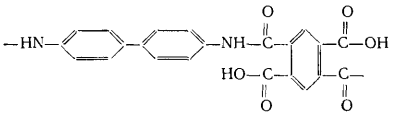
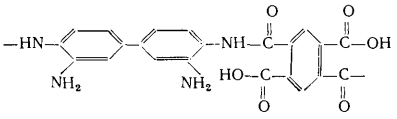
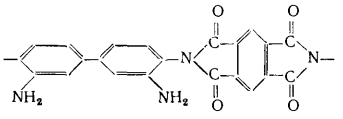
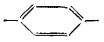


Figure 24. Dependence of T_g for a series of polymers on the ratio $\sum_i K_i^* / \sum_i \Delta V_i$.

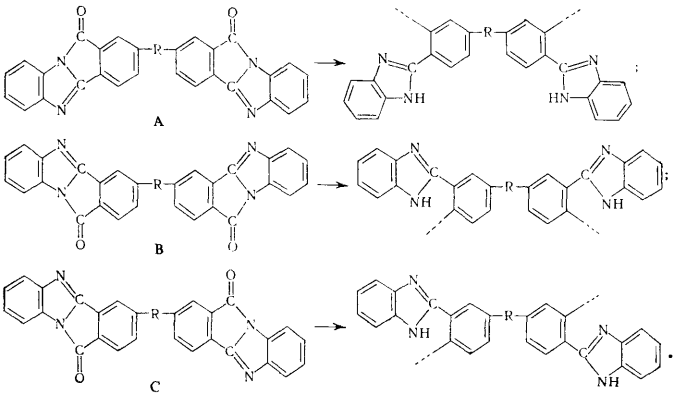
Another problem that can be solved by means of formula (8) is the calculation of glass points of polymers whose experimental determination presents great difficulties. Such are systems which undergo various types of chemical changes—thermal degradation, oxidation, cross-linking, cyclisation, etc.—when they are heated. This applies especially to heat-resistant polymers, in which such chemical changes may take place below the glass point. Table 2 gives calculated values for some of them, as well as for certain polyamide-esters, polyamino-acids, etc. that undergo rapid cyclisation.

Yet another use of the above scheme of calculation is to refine the chemical structure of a polymer whose glass

Table 2. Calculated glass points for polymers when experimental determination is difficult.

Polymer	$\sum_i \Delta V_i$, cm³ mole⁻¹	$\sum_i K_i^*$, cm³ mole⁻¹	T_g, °C (calc.)
	268.5	370.5	380±20
	208 8	266.6	242±15
	291.9	384.5	292±17
	259.7	310.3	154±13
	361.8	418.7	118±12
	180.7	232.0	251±16
	162.7	229.2	425±21
	203.6	271.9	316±18
	217.5	288.4	304±17
	194.3	285.8	532±24
	45.5	69.9	662±28
—[C≡C]—	14.8	21.5	493±23

point has been determined experimentally, as in a study [19] of the effect of chemical structure on the properties of polybenzazoles containing bulky substituents. These heat-resistant polymers may have an irregular arrangement of chains because of the possibility of geometrical (*cis–trans*) isomerism in the initial bisbenzoylenebenzimidazoles. With *meta*- or *para*-substitution the resulting polymers may in principle contain the structural units



It is difficult or almost impossible to determine the exact structure of such systems by the usual methods, so that the softening points of all the systems were calculated and compared with the experimental temperatures [19]. Experimental and calculated glass points showed good agreement when substitution occurred either in the *meta*-position or in *meta*- and *para*-positions. The first type of linking into chains may occur with the *cis*-isomer (A), and the second with the *trans*-isomer (B). Thus the polybenzazoles studied [19] evidently contain both structures and are mixtures of isomers. This is supported experimentally by the fairly wide melting range of the initial bisbenzoylenebenzimidazoles, despite their high purity. Analogous problems have also been solved [130].

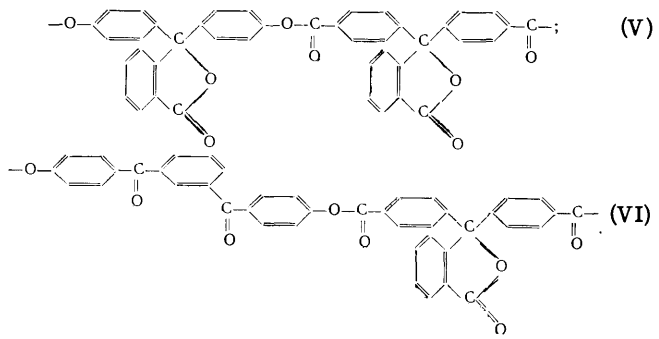
The chemical structure of a copolymer can also be determined by comparing calculated and experimental glass points. In several cases it is sufficient to apply formula (8), deduced on the assumption of approximately the same density of packing of macromolecules within monolithic amorphous systems. Differently constructed copolymers (random, block, various types of addition of units, etc.) may exhibit looser or denser packing of the macromolecules, which must be taken into account in the calculation. For this purpose Eqn. (8) can be rewritten

$$\lg T_g = \frac{k}{k_{av}} \cdot \frac{\sum_i K_i^*}{N_A \sum_i \Delta V_i} + A, \qquad (9)$$

where k is the actual packing coefficient and $k_{av} = 0.681$. Formula (9) will then give glass points higher or lower than the additive values depending on the composition, as is observed fairly often in practice. With copolymers not only the glass point but also the density must be determined experimentally, k calculated, and then T_g found from Eqn. (9). The chemical structure of the copolymer can be determined by comparing calculated and experimental glass points.

Furthermore, it is possible in several cases to estimate the contributions both of intermolecular and of intramolecular interactions to the glass point on passing from one copolymer to another. A series of copolymers and homopolymers was synthesised [129] from phenolphthalein,

3,3-diphenylphthalide-*p'p''*-dicarboxylic acid, and *m*-bis-*p'*-hydroxybenzoylbenzene. The homopolymers had the structures



(V)

(VI)

These polyesters, as well as all the copolymers, contained the same numbers of atoms and benzene residues, differing only in the numbers of attached phthalide rings. Passing from polymer (V) to polymer (VI) entailed not only diminished intermolecular interaction due to the phthalide ring but also a lower glass point because of diminished intramolecular interaction (steric factor). The contributions of each of these factors were estimated by means of formula (9), which for copolymers becomes

$$\lg T_g = \frac{k}{k_{av}} \cdot \frac{x_1\left(\sum_i \Delta V_i\right)_1 (\lg T_{g,1} - A) + x_2\left(\sum_i \Delta V_i\right)_2 (\lg T_{g,2} - A)}{x_1\left(\sum_i \Delta V_i\right)_1 + x_2\left(\sum_i \Delta V_i\right)_2} + A. \quad (10)$$

This showed that only half the difference $\Delta T = T_{g,1} - T_{g,2}$ was due to the decrease in the number of intermolecular bonds corresponding to the smaller number of phthalide groups, the rest being caused by rotation of a phthalide ring. The effective energy of intermolecular interaction in the presence of a phthalide ring was 9.4 kcal mole^{-1}.

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Comparison of the whole set of properties of heat-resistant aromatic polymers with those of ordinary polymers having relatively inflexible chains indicates that increasing the rigidity of the chain and saturating it with aromatic rings lead to the expected rise in the glass point, but this is accompanied by qualitative changes in all the other properties. Passing to heat-resistant aromatic polymers (e.g. various types of polyheteroarylenes) leads to a significant increase in the maximum mechanical stresses that the polymeric material is able to withstand in articles not only at high but also at ordinary temperatures. The explanation is not that the fixed test temperature lies at different distances from the glass point with different compounds: if this were the reason, application of the principle of corresponding states would yield the same tensile strength or limit of forced elasticity at the reduced temperature. However, this does not occur, since the temperature dependence of the forced rubberlike elasticity is indistinct at temperatures sufficiently below the glass point, and these relations cannot be superimposed merely by displacement along the temperature axis. Hence the reason for the increased strength lies in the actual nature of the polymer chain saturated with aromatic rings.

The difference between the mechanical properties of flexible-chain and rigid-chain aromatic polymers becomes especially clear in prolonged observations under conditions of stress relaxation. Such relaxation is considerably less marked with rigid-chain than with flexible-chain systems, which is responsible for the great difference in the mechanical stresses that these systems are able to withstand at a given temperature. Thus the synthesis of heat-resistant aromatic polymers not only extends the temperature range of performance but also increases significantly the mechanical stresses under which performance is maintained at lower temperatures.

Another characteristic feature of heat-resistant systems is an extraordinarily large optical stress coefficient C_σ, whose values for polyheteroarylenes exceed those for ordinary polymeric glasses (polystyrene, polymethacrylates, etc.) by factors of 10–1000. This means that even very small mechanical stresses cause large double refraction in them, which is of great practical importance, since the use of such materials in the photoelastic method enables the pattern of stress distribution to be obtained with extremely small deformations, i.e. under conditions under which Hooke's law is best obeyed.

The next interesting feature of heat-resistant aromatic polymers is a multitude of relaxation transitions, which plays a very important part in shaping the whole set of mechanical and other physical properties. In the Reviewers' opinion, especial interest attaches to the static methods that have been discovered for investigating the transitions, which largely determine the temperature ranges of performance, i.e. the heat resistance of the polymers.

Another curious feature of heat-resistant polyheteroarylenes is their capacity for considerable (10–20%) deformation at very low temperatures (down to that of liquid nitrogen) [5,6,72,131]. Hence heat-resistant aromatic polymers are able to satisfy a requirement for a polymeric material that is capable of non-brittle fracture not only at high but also at low temperatures.

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Kinetics and Mechanism of the Decomposition of Organic Hydroperoxides in the Presence of Transition Metal Compounds

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The principal features of the homogeneous-catalytic decomposition of hydroperoxides in the presence of variable-valence metal compounds are examined and kinetic and physicochemical evidence for the formation of intermediate catalyst-hydroperoxide complexes and their subsequent decomposition into free radicals and molecular products is presented. Factors influencing the change in the mode of decomposition of the hydroperoxide are analysed and a special section is devoted to the catalysis of the decomposition of hydroperoxides by soluble molybdenum, vanadium, and tungsten compounds and also to the mechanism of the catalytic epoxidation of olefins by bound oxygen.
The bibliography includes 134 references.

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I. INTRODUCTION

The theory of liquid-phase oxidation processes of hydrocarbons has been developed in fair detail, to a large extent by Emanuel' and his school[1,2]. The problem of the influence of various additives on the liquid-phase oxidation, the solution of which would permit the inhibition of undesirable oxidation process[3,4] or the acceleration of the oxidation and would make the latter more selective as a result of the employment of homogeneous or heterogeneous catalysts[5,6], has now become of primary importance.

The problems of the mechanism of homogeneous-catalytic oxidation reactions have been analysed fairly recently in a number of reviews[7-9]. The mechanism of one of the principal stages in the oxidation of hydrocarbons —the decomposition reactions of hydroperoxides and chain branching in the presence of homogeneous catalysts— are discussed below. Studies on the mechanism of the homogeneous-catalytic decomposition of hydroperoxides are important not only from the standpoint of the further development of the theory of liquid-phase oxidation but also for the determination of the general characteristics of homogeneous catalysis, since the decomposition of hydroperoxides constitutes a convenient model for a quantitative investigation of the influence of the structures of the hydroperoxide and the catalyst on the rate and mechanism of the process. In view of the extensive data available for the decomposition of peroxide compounds, we shall consider only the most characteristic features of the mechanism of the decomposition of organic hydroperoxides.

II. RADICAL DECOMPOSITION

Modern ideas concerning the mechanism of the catalytic action of transition metal compounds in hydroperoxide decomposition reactions are based on the mechanism proposed by Haber and Weiss[10], according to which the hydroperoxide alternatively behaves as an oxidant and as a reductant in the reaction with the reduced or oxidised form of the metal respectively:

$$ROOH + M^{n+} \rightarrow RO^{\cdot} + OH^{-} + M^{(n+1)+}; \quad (1)$$

$$ROOH + M^{(n+1)+} \rightarrow ROO^{\cdot} + H^{+} + M^{n+}. \quad (2)$$

The alternation of reactions (1) and (2) ensures the constancy of the ratio of the different valence forms of the catalyst in the course of the process and is responsible for the catalytic effect. Depending on the type of the hydroperoxide and the nature of the catalyst, the number of molecules of the hydroperoxide decomposed per catalyst molecule may be up to 1000 and more. This hydroperoxide decomposition mechanism in non-aqueous media has been confirmed in a number of investigations[7,8].

When the compounds of metals which can exist typically in more than two valence states are used as the catalysts, the decomposition of hydroperoxides may involve a more complex mechanism. Thus the decomposition of hydroperoxides in the presence of rhodium compounds can lead to the formation in the system of three valence forms: rhodium(I), rhodium(II), and rhodium(III). It has been suggested that the process is catalysed by the rhodium(II)–rhodium(III),[11] rhodium(I)–rhodium(II),[12] or rhodium(I)–rhodium(III)[13] pairs. However, in the latter case the process does not proceed via the two-electron mechanism proposed by the authors:

$$Rh(I) + 2\,ROOH \rightarrow Rh(III) + 2\,RO^{\cdot} + 2\,OH^{-},$$
$$Rh(III) + 2\,ROOH \rightarrow Rh(I) + 2\,ROO^{\cdot} + 2H^{+},$$

but is accompanied by the formation (at least as an intermediate) of a rhodium(II) species, which may be identified[12] by its ESR spectrum in the decomposition of cumenyl hydroperoxide in the presence of $Rh(I)(PPh_3)_3$.COCl.

The valence forms of the metal do not necessarily change when the hydroperoxide is involved in stages (1) and (2). Metals in the highest valence state can react rapidly with hydroperoxide decomposition products and also with the solvent[1,2,14–16]. Thus it has been suggested[17] that, in the oxidation of aldehydes in an aqueous phase, the cobalt(III) → cobalt(II) transition takes place with participation of benzaldehyde; the reaction of cobalt(III) with C_6H_5COOH is extremely slow, although in a later study[18] the possibility of reducing cobalt(III) by perbenzoic acid was noted. Nickel(III) reacts rapidly with benzaldehyde[18]. The rate of the valence transformation manganese(III) → manganese(II) increases appreciably in the presence of aldehydes[19]. The involvement of aldehydes in the degenerate branching of chains in the catalytic oxidation of alkanes has been postulated[20]. The involvement of alcohols, ketones, and acids in oxidation-reduction reactions with participation of metal ions is also extremely likely. For example, the steady-state concentration of manganese(III) in the catalytic decomposition of t-butyl hydroperoxide falls as the process develops, which may be due to the reduction of manganese(III) by the ROOH decomposition products—methyl alcohol or acetone[19]. It has been shown[21–23] that, in the decomposition of acyl hydroperoxides cobalt(II) is almost wholly converted into the tervalent form. In the decomposition of alkyl hydroperoxides cobalt is also mainly present in the tervalent form, although the rate of the transition cobalt(II) → cobalt(III) is much lower than for acyl peroxides. In the presence of organic acids cobalt is present only in the bivalent form during the reaction. When cobalt(III) is used as the catalyst in the presence of organic acids, the transition cobalt(III) → cobalt(II) takes place rapidly. The oxidation of alcohols, ketones, and acids by cobalt(III) ions has been studied in a number of investigations[24–26].

The ratio of the valence forms of the catalyst is determined by the different reactivities of the oxidised and reduced forms of the metal ion in the reaction with the hydroperoxide or other products[21,27].

The formation of free peroxy-radicals in the decomposition of hydroperoxides in the presence of variable-valence metal compounds has been demonstrated[28–30]. The ESR spectra of free peroxy-radicals have been observed in the decomposition of t-butyl, cumenyl, diphenylethyl, and triphenylmethyl hydroperoxides in the presence of cobalt compounds[31]. The method of inhibitors has been used to identify hydroperoxides and to measure the rates of their radical decomposition[5,31].

Although it has been suggested in the majority of studies that the interaction of the reduced form of the catalyst with the hydroperoxide [reaction (2)] entails the formation of the hydroxide ion and a free alkoxy-radical $RO^{\cdot}$, in some instances, for example in the decomposition of tetralinyl hydroperoxide in the presence of cobalt carboxylates, the composition of the ROOH decomposition products can be explained by simply postulating the formation in this process of an $OH^{\cdot}$ radical and an RO^{-} ion[33–35].

Kinetic studies on the decomposition reactions of hydroperoxides have shown that the overall order of the reaction with respect to the catalyst and the hydroperoxide depends on the solvent and the nature and concentration of the hydroperoxide and the catalyst and can vary from zero to two. Second-order decomposition of hydroperoxide with respect to the catalyst and first-order decomposition with respect to the hydroperoxide have been observed in the decomposition of tetralinyl hydroperoxide in xylene and acetic acid[36–39], in the decomposition of t-butyl hydroperoxide in the presence of cobalt(II) ethylenediaminetetraacetate[40], and in the decomposition of n-decyl hydroperoxide in the presence of cobalt stearate[41].

There have been numerous instances where the order of the reaction with respect to the catalyst proved to be 1 or 1.5;[5,32] in some cases the reaction order varies during the process or depends on the initial concentration of the hydroperoxide or the catalyst. Thus the decomposition of tetralinyl hydroperoxide in the presence of chromium, copper, and cobalt oleates is a first-order reaction with respect to the hydroperoxide, while the order with respect to the catalyst varies from 0.5 to 0.7.[23] The decomposition of cumenyl hydroperoxide in chlorobenzene in the presence of cobalt salts is a first-order reaction with respect to ROOH and the catalyst[42–45]. A linear variation of the rate of decomposition with catalyst concentration was observed in the decomposition of hydroperoxides by cobalt salts in alcohols[46] and by cobalt complexes in chlorobenzene and benzene[47,48]. In the decomposition of t-butyl hydroperoxide in chlorobenzene in the presence of cobalt 2-ethylhexanoate the order of the reaction with respect to the catalyst depends strongly on its concentration. At 20°C the order of the reaction with respect to the catalyst increases from 1 to 1.6 with increase of the salt concentration from 1.3×10^{-5} to 8.4×10^{-5} M and then falls as

the salt concentration rises further. At 0°C the order of the reaction with respect to the catalyst diminishes with increasing salt concentration[36].

In the inhibited decomposition of t-butyl hydroperoxide in acetic and butyric acids and their mixtures with chlorobenzene the order of the reaction with respect to cobalt acetate is close to unity[44,49], while for the non-inhibited reaction it is greater than unity[44]. A reaction order greater than unity has been observed in other investigations[40,43,50-54].

The order of the hydroperoxide decomposition reaction with respect to ROOH also depends on the nature and concentration of the latter. Thus in the decomposition of ethylphenyl hydroperoxide in the presence of copper stearate, the order of the reaction with respect to ROOH was unity[55], while in the decomposition of n-decyl hydroperoxide it was 2, falling to zero with increase of [ROOH].[56,57] In most of the cases investigated the reaction order with respect to ROOH tends to zero with increase of the hydroperoxide concentration[5,47,48,55-58].

Various mechanisms have been proposed for the decomposition of hydroperoxides in the presence of cobalt, copper, and manganese salts[36,49,59-63]. In certain instances the formation of organometallic peroxide compounds decomposing subsequently into free radicals[64]:

$$\mathrm{ROOH} + \mathrm{M}^{n+}\mathrm{X} \rightarrow \mathrm{ROOM}^{n+} + \mathrm{HX}, \quad (3)$$

$$\mathrm{ROOM}^{n+} \rightarrow \mathrm{RO}^{\cdot} + \mathrm{OM}^{(n+1)+} \quad (4)$$

$$\searrow \mathrm{ROO}^{\cdot} + \mathrm{M}^{(n+1)+}, \quad (5)$$

(X represents the anion) or oxidative addition of ROOH to the catalyst:

$$\mathrm{ROOH} + \mathrm{M}^{n+} \rightarrow \mathrm{ROM}^{(n+2)+}\mathrm{OH} \quad (6)$$

with subsequent decomposition of the complex formed were suggested.

The decrease of the order of the hydroperoxide decomposition reaction with respect to ROOH with increasing concentration of the latter was explained in terms of intermediate formation of a complex by the hydroperoxide and the catalyst[5,32]:

$$n\,\mathrm{ROOH} + m\,\mathrm{M}^{n+} \xrightarrow{k_1} n\,\mathrm{ROOH}\cdot m\,\mathrm{M}^{n+}. \quad (7)$$

The resulting complex is unstable and decomposes into the reaction products:

$$n\,\mathrm{ROOH}\cdot m\,\mathrm{M}^{n+} \xrightarrow{k_1} \mathrm{RO}^{\cdot} + \mathrm{OH}^{-} + \mathrm{M}^{(n+1)+} + (n-1)\,\mathrm{ROOH} + m-1)\,M^{n+}. \quad (8)$$

The reduced form of the catalyst also decomposes via the intermediate formation of the complex:

$$n_1\,\mathrm{ROOH} + m_1\,\mathrm{M}^{(n+1)+} \rightleftarrows n_1\,\mathrm{ROOH}\cdot m_1\,\mathrm{M}^{(n+1)+} \rightarrow \mathrm{ROO}^{\cdot} + \mathrm{H}^{+} + \mathrm{M}^{n+} + (n_1-1)\,\mathrm{ROOH} + (m_1-1)\,\mathrm{M}^{(n+1)+}. \quad (9)$$

The mechanism of reactions (7)–(9) yields a simple expression of the Michaelis–Menten type for the variation of the rate of decomposition with the concentrations of the hydroperoxide and the catalyst[5,32]. For $n = m = n_1 = m_1 = 1$, the equation is

$$W = \frac{Kk_1\,[\mathrm{ROOH}]\,[M^{n+}]}{1 + K\,[\mathrm{ROOH}]} \quad (10)$$

and makes it possible to determine the complex formation constant K and the rate constant k_1 for the decomposition of the complex into free radicals.

The second order with respect to the catalyst[41,65] may be due to the two-stage process

$$\mathrm{ROOH} + \mathrm{CoX}_2 \rightleftarrows \mathrm{ROOH}\cdot\mathrm{CoX}_2,$$
$$\mathrm{ROOH}\cdot\mathrm{CoX}_2 + \mathrm{CoX}_2 \rightarrow \mathrm{RO}^{\cdot} + \mathrm{CoX}_2\mathrm{OH} + \mathrm{H}_2\mathrm{O} + \mathrm{CoX}_2.$$

It has been suggested that the first order with respect to the catalyst in acetic acid[38,65] is due to the involvement of the dimeric form of cobalt acetate in the reaction:

$$2\mathrm{CoAc}_3\cdot\mathrm{AcH} \rightleftarrows (\mathrm{CoAc}_3)_2\cdot\mathrm{AcH} + \mathrm{AcH},$$
$$\mathrm{ROOH} + \mathrm{AcH} \rightleftarrows \mathrm{ROOH}\cdot\mathrm{AcH},$$
$$(\mathrm{CoAc}_3)_2\cdot\mathrm{AcH} + \mathrm{ROOH} \rightarrow \text{radicals}.$$

The second-order with respect to the hydroperoxide in the presence of copper salts may be attributed to the formation of the hydroperoxide–catalyst complexes having the composition $\mathrm{CuX}_2.2\mathrm{ROOH}$ [56,57] or $2\mathrm{CuX}_2.2\mathrm{ROOH}$.[66]

The formation of catalyst–hydroperoxide complexes has been confirmed by various physicochemical methods: spectrophotometrically in the decomposition of cumenyl hydroperoxide in the presence of bis-[*N*-(2-hydroxy-3-methoxybenzylidene)aniline] cobalt[47] and of ethylphenyl hydroperoxide in the presence of copper stearate[55], the formation of copper 2-ethylhexanoate complexes with t-butyl hydroperoxide[66] and of bis-(α-thiopicolinanilide)-copper with ethylphenyl hydroperoxide[67] has been demonstrated by ESR, and the formation of complexes of cumenyl hydroperoxide with cobalt and nickel chelates has been demonstrated by NMR.[68,69] In the last case the formation of complexes was inferred from the chemical shifts of the OH protons of the hydroperoxides and it may be regarded as established that (at least for the systems investigated) ROOH does not add as a result of ligand exchange via reactions (3) or (6), as postulated by Waters[64]. The hydroperoxide is coordinated to the central metal ion via the oxygen atom of the hydroxy-group[69].

The equilibrium constants for the formation of the complexes have been calculated by Eqn. (10) for a large number of catalysts and hydroperoxides[70]. It has been shown for the decomposition of cumenyl hydroperoxide in the presence of substituted bis-[*N*-aryl-*N*-(2-hydroxy-3-methoxybenzylidene)amine]cobalt complexes that the introduction of electron-donating substituents into the ligand has only a slight influence on the rate constant for the decomposition of the catalyst–hydroperoxide complex and leads mainly to a change in the equilibrium constant for the formation of the complex[58].

Quantitative evidence for the role of complex formation in the catalytic decomposition of hydroperoxides is provided by the agreement[68] between the equilibrium constants for the formation of cobalt chelates with cumenyl hydroperoxide determined by two independent methods: from the chemical shift of the OH proton of the hydroperoxide in the presence of the catalyst and by a kinetic method from the dependence of the rate of decomposition of ROOH on its concentration using Eqn. (10). This suggested that the formation of the complexes, identified by a physicochemical method, in the catalyst–hydroperoxide system is indeed an intermediate stage in the catalysis.

The decrease of the reaction order with respect to the catalyst with increase of its concentration has been explained in some investigations by the aggregation of the catalyst[38,56,66,71] or by the interaction of one of its valence forms with free radicals[72]. The latter hypothesis can explain the relative decrease of the rate of reaction only in the presence of a chain mechanism of the decomposition of ROOH. The study of the decomposition of cumenyl hydroperoxide in the presence of copper stearate complexes with *o*-phenanthroline (*o*-phen) in benzene and chlorobenzene showed that there is no chain mechanism of the hydroperoxide decomposition reaction and that the decrease of the reaction order with respect to the catalyst from 1 to 0 with increase of [CuSt_2.*o*-phen] is not related to the formation of micelles[73].

It has been suggested that deactivation of the catalyst in the process occurs owing to the formation of inactive dinuclear complexes. The process mechanism involves stages in which copper(I) complexes of the hydroperoxide are formed:

$$\text{Cu(II)} \cdot o\text{-phen} \xrightarrow{\text{ROOH}} \text{Cu(I)} \cdot o\text{-phen} \quad ,$$

$$\text{Cu(I)} \cdot o\text{-phen} + \text{ROOH} \rightarrow \text{Cu}^{\delta+}\text{(I)}\ o\text{-phen}\ \overset{\delta-}{\text{ROOH}} \quad .$$

This is followed by the reactions of the complexes $\overset{\delta+}{\text{Cu(I)}}(o\text{-phen})(\overset{\delta-}{\text{ROOH}})$ with the catalyst (catalyst deactivation) and the hydroperoxide (catalytic stage). The mechanism proposed explained quantitatively the kinetic curves for the decomposition of the hydroperoxide and also the variation of the rate of decomposition of ROOH with the concentrations of the catalyst and the hydroperoxide.

III. MOLECULAR DECOMPOSITION

The so called "molecular" mechanism of the decomposition of the hydroperoxide, which leads to the formation of non-radical products, has been observed in the decomposition of many organic hydroperoxides in the presence of various organometallic catalysts.

This decomposition mechanism was postulated initially on the basis of data for the influence of variable-valence metal compounds on the oxidation of hydrocarbons[74]. The increase of the rate of decomposition of the hydroperoxide via the molecular mechanism lowers the rate of formation of free radicals in the system. In certain cases, where the rate of formation of the radicals in the presence of the catalyst is lower than the rate of their formation in the absence of the catalyst, the introduction of organometallic compounds can lead to the appearance of induction periods. The inhibition of the oxidation of hydrocarbons in the presence of nickel, cobalt, platinum, and palladium dithioketonates, which are effective catalysts of the decomposition of hydroperoxides, is treated from precisely this standpoint[75].

This treatment of the inhibiting effect of variable-valence compounds is not unambiguous, since almost all the compounds employed are radical acceptors and may inhibit the oxidation not only owing to the decomposition of ROOH but also owing to the increase of the rate of chain termination[76-78]. Direct evidence for the occurrence of the molecular mechanism in the decomposition of the hydroperoxide in the presence of the catalyst was obtained with the aid of inhibitors[32,56]. It was shown that, in the decomposition of n-decyl hydroperoxide in the presence of copper stearate, the rate of consumption of ROOH is significantly higher than the rate of consumption of the inhibitor, which is equal to the rate of formation of free radicals. An appreciable molecular decomposition of the hydroperoxide was demonstrated in a study of the decomposition of tetralinyl hydroperoxide under the influence of cobalt salts in various solvents[34,35].

The contribution of the molecular decomposition of the hydroperoxide depends significantly on the nature of the catalyst and the hydroperoxide[79]. Thus in the presence of cobalt stearate t-butyl hydroperoxide decomposes at 50°C in chlorobenzene only into free radicals; the rates of decomposition of tetralinyl[35] and cumenyl[79] hydroperoxides into free radicals under the same conditions are 1.2 and 36% of the overall rate of decomposition of ROOH respectively; the contributions of the radical pathways to the decomposition of α-phenylethyl hydroperoxide in the presence of tin 2,2'-thiobis-[4-methyl-6-(α-methylbenzyl)-phenoxide] and 2,2'-thiobis-(6-t-butyl-4-methylphenoxide) are 0.1 and 3.5% respectively[80]. When the metal in the catalyst is changed, the relative contributions of the molecular and radical mechanisms of the decomposition of ROOH also change. In the presence of $CoSt_2$, n-decyl hydroperoxide decomposes only via the radical pathway[41], while in the presence of $CuSt_2$ the contribution of the molecular decomposition is 20–50% [56,57] of the overall rate of decomposition of ROOH. The contribution of the radical decomposition of t-butyl hydroperoxide is 100% in the presence of $CoSt_2$ [81] and 4–10% in the presence of manganese stearate[19].

The study of the dependence of the rates of decomposition of hydroperoxides and of the consumption of the inhibitor on the catalyst and hydroperoxide concentrations established that in all cases the molecular decomposition of the hydroperoxide proceeds, like the radical decomposition, via a stage involving the formation of catalyst–hydroperoxide complexes. Determination of the thermodynamic characteristics and compositions of these complexes from the rates of the molecular and radical decompositions of ROOH showed that, in the decomposition of cumenyl, n-decyl, tetralinyl, and α-phenylethyl hydroperoxides in the presence of copper, cobalt, and nickel compounds, both mechanisms of the decomposition of the hydroperoxides involve the formation of the same complexes[79,82-84].

Kinetic data for the variation of the rates of decomposition of hydroperoxides with their concentrations and with that of the catalyst made possible in many instances the calculation of the individual rate constants for the decomposition of the catalyst–hydroperoxide complexes into free radicals (k_r) and the molecular products (k). It was found that the k_r are as a rule associated with very low pre-exponential factors[70]. The relative contributions of the molecular and radical mechanisms of the decomposition of the hydroperoxide depend markedly on the viscosity of the medium—with increase of η, the contribution of the molecular decomposition of ROOH increases, but the overall rate remains unchanged. The variation of the ratio k_r/k is described by the Stokes–Einstein formula, which leads to the conclusion that the role of diffusion processes in the mechanism of the catalytic decomposition of ROOH is important[79].

The kinetic data obtained suggested a mechanism for the molecular decomposition of the hydroperoxide in which the "cage effect" of the solvent plays an important role[19,79,82-86]. The radicals formed in the decomposition of the complex MX_2.ROOH can either recombine in the solvent cage (molecular decomposition of the hydroperoxide) or can diffuse from the cage (radical decomposition):

$$MX_2 + ROH \rightleftarrows MX_2 \cdot ROH \rightarrow [MX_2OH,\ RO]$$

$$RO^{\cdot} + MX_2OH \qquad MX_2 + H_2O + R'COR'' \quad .$$

It has been suggested[34] for the decomposition of tetralinyl hydroperoxide in the presence of cobalt salts that ROOH decomposes when the complex MX_2.ROOH reacts with the hydrocarbon as follows:

$$[MX_2 \cdot ROOH] + R'H \rightarrow [MX_2^{\cdot} \ \ldots\ R''] + \text{product.} \qquad (11)$$

The relative contributions of the molecular and radical mechanisms of the decomposition of ROOH are then determined by the ratio of the rates of recombination of the radicals R'' within the cage and by the number of

radicals released from the cage when the complex $MX_2 \ldots R''$ reacts with a second R'H molecule:

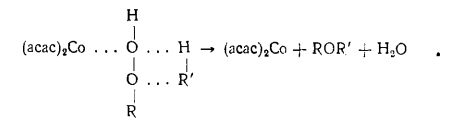
$$[\dot{M}X_2 \ \ldots \ R''] + R'H \rightarrow 2R'' + MX_2 + \text{product}. \qquad (12)$$

In this mechanism of the decomposition of the hydroperoxide an increase of the rate of consumption of ROOH [stage (11)] and of the contribution of the radical ROOH decomposition mechanism [stage (12)] was to be expected with decrease of the C–H bond strength in the hydrocarbon solvent.

This mechanism of the molecular decomposition of the hydroperoxide does not hold in the decomposition of cumenyl hydroperoxide (CHP) in the presence of cobalt acetylacetonate [$Co(acac)_2$].[86] In this case the rate of decomposition of CHP is almost independent of the solvent and the contribution of the molecular decomposition of ROOH increases in the sequence benzene < ethylbenzene < tetralin, i.e. with decrease of the C–H bond strength in the hydrocarbon. This suggested a more complex role of the solvent in the ROOH decomposition mechanism. As in inert solvents, in the presence of hydrocarbons the consumption of hydroperoxides is determined by the stage

$$Co(acac)_2 \cdot ROOH \rightarrow [\overset{\delta+}{Co}(acac)_2; \ \overset{\delta-}{ROOH}].$$

The $[\overset{\delta-}{Co}(acac)_2, \ \overset{\delta+}{ROOH}]$ species formed reacts further with RH to form non-radical products, most probably ethers. Such interaction can proceed via a stage involving the formation of ternary complexes:



This pathway, involving a bimolecular interaction of the hydroperoxide with the hydrocarbon, is a characteristic feature of the catalytic decomposition of the hydroperoxide and is due to the activation of ROOH when it is bound in a complex with the catalyst (probably as a result of partial electron transfer). In the absence of a catalyst the hydroperoxide interacts with the hydrocarbon to form only free radicals as the reaction products[1].

IV. INDUCED CHAIN DECOMPOSITION

The decomposition of the hydroperoxide induced by free radicals (chain decomposition of the hydroperoxide) is largely characteristic of the non-catalytic decomposition, which is probably associated to a considerable extent with the marked increase of the rate of formation of the radicals and the corresponding decrease of chain length in the presence of the catalyst.

The hypothesis of an appreciable contribution of the decomposition of the hydroperoxide induced by free radicals was put forward for the first time in a study of the kinetics of the oxidation of n-decane in the presence of manganese(II) stearate[87]. Direct methods using inhibitors of free-radical processes demonstrated the occurrence of the chain pathway in the decomposition of t-butyl and cumenyl hydroperoxides in the presence of cobalt acetate in a chlorobenzene–acetic acid mixture[88], of cumenyl hydroperoxide in benzene in the presence of substituted *N*-aryl-*N*-(2-hydroxy-3-methoxybenzylidene)aminocobalt complexes[89], and of tetralinyl hydroperoxide in the presence of cobalt acetate in tetralin[38].

The occurrence of the chain pathway in the hydroperoxide decomposition reaction depends strongly on the nature of the catalyst. Thus, according to data obtained by the method of inhibitors using ionol as the inhibitor[72], in the presence of iron-phthalocyanine t-butyl hydroperoxide decomposes via the chain mechanism, while in the presence of cobalt salts there is no chain decomposition of the hydroperoxide.

This influence of the nature of the catalyst on the mode of decomposition of the hydroperoxide may be one of the manifestations of the dual function of the catalyst discovered in 1959 by Emanuel' and coworkers[90], which consists in the ability of the catalyst not only to generate free radicals but also to participate in the chain termination reaction. It was shown in later studies that metal compounds can interact with both peroxy-[77,91] and alkoxy-radicals[92,93] formed in the decomposition of hydroperoxides. In hydrocarbon media, where there is a possibility of chain transfer to the solvent, the interaction of metal compounds with free alkyl radicals may play an important role[94].

Unfortunately in the presence of the catalyst the use of inhibitors greatly alters the properties of the catalyst itself, for example as a result of complex-formation effects. The inhibition of the catalytic decomposition of the hydroperoxide by the addition of the inhibitor can be caused in this case not only by the suppression of the chain decomposition of the hydroperoxide but also by the "poisoning" of the catalyst. Furthermore, there is a possibility of oxidation-reduction reactions between one of the forms of the catalyst and the inhibitor, which leads to a change in the relative amounts of the different valence forms of the catalyst, and hence in the measured rate of decomposition of ROOH. For this reason, the available information in the literature concerning the occurrence of the induced decomposition of ROOH in the presence of the catalyst is frequently contradictory. Thus Skibida et al.[35] showed, in contrast to Kamiya et al.[38], that tetralinyl hydroperoxide does not undergo chain decomposition in benzene in the presence of $CoSt_2$. One cannot rule out the possibility that the ionol employed by Kamiya et al.[38] as the inhibitor interacted with the catalyst in the highest valence state, which has in fact been demonstrated, for example by Gernet et al.[95]

The occurrence of the chain decomposition of ROOH is determined to a large extent by the nature of the alkyl radical and the hydroperoxide. t-Butyl and cumenyl hydroperoxides decompose in the presence of cobalt salts via the chain mechanism, which is apparently not characteristic of the decomposition of triphenylmethyl and diphenylethyl hydroperoxides[30,43,88].

In certain cases conclusions concerning the occurrence of the induced decomposition of the hydroperoxide are reached on the basis of a comparison of the rates of the overall decomposition of hydroperoxides having different structures. The rate of decomposition of the primary n-butyl hydroperoxide in chlorobenzene in the presence of cobalt 2-ethylhexanoate is lower than the rate of decomposition of t-butyl hydroperoxide under the same conditions, which suggested a greater contribution of the chain decomposition of the tertiary hydroperoxide. This hypothesis is consistent with the change in the reactivity of the free radicals: the rate of recombination increases on passing from the t-butyl to the n-butyl-peroxy-radical; consequently the probability of chain propagation diminishes. However, the above influence of the nature of the hydroperoxide on the rate of its decomposition can be caused also by the influence of the structure of the radical

on the rate of the primary decomposition of the hydroperoxide into free radicals. Furthermore, there is also a possibility of a change in the mechanism of the radical decomposition of ROOH. As stated above, the primary step in the hydroperoxide decomposition reaction may lead to the formation of a free hydroxy-radical and an alkoxide anion and not a hydroxide ion and an RO· radical[33,35,36]. The chain decomposition of ROOH can then be induced by the OH· radical[33,36,96]. It has been suggested[97] that the decomposition products of t-butyl hydroperoxide are formed when free peroxy-radicals react with the hydroperoxide–catalyst complex.

The available factual data suggest that the chain decomposition of the hydroperoxide in the presence of the catalyst is mainly characteristic of tertiary hydroperoxides in aprotic media.

V. THE INFLUENCE OF SOLVENTS ON THE CATALYTIC DECOMPOSITION OF HYDROPEROXIDES

As in the thermal decomposition of hydroperoxides, the rate of their decomposition in the presence of catalysts is largely determined by the nature of the solvent. A study of the decomposition of cumenyl hydroperoxide in different solvents catalysed by cobalt abietate[43] showed that the rate of decomposition and the effective activation energy greatly depend on the solvent. The above solvents can be arranged in the sequence nonane < toluene < chlorobenzene < benzene in terms of the rate of decomposition. The activation energies fall in the same sequence from 21 kcal mole^{-1} for nonane to 13 kcal mole^{-1} for benzene.

The rate of decomposition of the hydroperoxide varies even more in the presence of oxygen-containing compounds. The addition of dimethylphenylmethanol to give a concentration comparable to that of t-butyl hydroperoxide reduces the rate of decomposition of the latter by a factor of four in the presence of cobalt abietate[98]. The rate of decomposition of cumenyl hydroperoxide in the presence of dimethylphenylmethanol (25% relative to the hydroperoxide employed) decreases almost by a factor of two, while α-tetralinone strongly inhibits the decomposition of tetralinyl hydroperoxide[36]. In the decomposition of cumenyl hydroperoxide by cobalt salts in alcoholic solutions a deviation was observed from the equation for first-order kinetics with respect to the hydroperoxide[46]. Acetophenone and dimethylphenylmethanol inhibit the decomposition of the hydroperoxide in the presence of copper stearate[55].

Organic acids as a rule strongly inhibit the decomposition of hydroperoxides in the presence of homogeneous catalysts; low-molecular-weight acids exhibit the strongest influence[38,99,100]. The rate of decomposition of tetralinyl hydroperoxide in a mixed solvent consisting of benzene and an organic acid falls in proportion to the square of the concentration of the acid[38,99]. A detailed study of the decomposition of cumenyl hydroperoxide catalysed by cobalt carboxylates in chlorobenzene, organic acids, and their mixtures has been carried out[31]. With increase of the concentration of acid in the solution, the rate constant for the decomposition of the hydroperoxide falls. The hydroperoxide decomposition rate constant in the presence of cobalt(II) oenanthate decreases by a factor of 90 on passing from a solvent containing 6% of butyric acid to pure butyric acid. The apparent activation energy rises from 12 kcal mole^{-1} in chlorobenzene to 22 kcal mole^{-1} in the presence of butyric acid, but depends only slightly on the amount of added acid.

The inhibiting effect of acetic and 2-ethyloenanthic acids on the rate of decomposition of t-butyl hydroperoxide catalysed by cobalt salts has been demonstrated[100]. The decrease of the catalytic activity of nickel stearate in the decomposition of α-phenylethyl hydroperoxide in the presence of acetic acid has also been established[101]. Aliphatic alcohols, ketones, and acids greatly reduce the rate of decomposition of n-decyl hydroperoxide in the presence of copper stearate[102].

The above data show that such influence of the solvent can be due to several causes.

1. Since in the majority of the studies quoted the influence of the solvent on the overall rate of decomposition of the hydroperoxide was considered, the observed influence of hydrocarbon solvents is possibly associated with a change in the contribution of the induced decomposition of the hydroperoxide owing to the change in the reactivity of the radicals caused by the involvement of the solvent in the chain transfer reaction.
2. Many solvents, particularly alcohols, ketones, and acids, can alter the relative amounts of the different valence forms of the catalyst as a result of reaction with the highest valence form of the metal. This effect also leads to an alteration of the rate of decomposition of the hydroperoxide.
3. Finally, the possible formation of complexes by the metal with the solvent may be a significant factor influencing the efficiency of the catalyst. Below we shall consider in somewhat greater detail the role of the formation of complexes of the catalyst and the solvent in the mechanism of the homogeneous-catalytic decomposition of hydroperoxides.

The decrease of the induction period in the oxidation of cyclohexanone catalysed by manganese stearate following the addition of benzoic acid and the acceleration of the oxidation in the presence of butyric acid have been attributed[103] to the formation of a complex of the acid and the catalyst, as a result of which the latter is activated.

The influence of acids on catalytic oxidation processes depends on the structure of the catalyst employed, particularly on the metal ion. For example, the addition of caprylic acid activates cobalt stearate but passivates manganese caprylate in the oxidation of cyclohexane[104]. It has been suggested that the hydroperoxide decomposes via the following mechanism in the coordination sphere of the metal:

$$M[X_5, ROOH]^{n+} \rightarrow M[X_5, (OH^-)]^{(n-1)+} + RO^{\cdot}.$$

In the presence of acids there is a possibility of the simultaneous coordination of hydroperoxide and acid molecules to the metal ion:

$$M[X_5, ROOH, R'COOH]^{n+} \rightarrow M[X_4, (R'COO), (H_2O)]^{(n-1)+} + RO^{\cdot}.$$

Depending on the relative rates of these reactions, the presence of the acid in the coordination sphere of the metal can either inhibit or accelerate the decomposition of the hydroperoxide and can lead to a corresponding retardation or acceleration of the oxidation reaction.

There are many fewer examples of the suppression of the catalytic activity of homogeneous catalysts by the addition of compounds capable of forming complexes with organometallic compounds. The decrease of the rate of oxidation of cyclohexane in the presence of cobalt stearate has been attributed[105] to the formation in the system of polar substances such as cyclohexanol or water, which

block the catalyst molecules and reduce the rate of initiation thereby. The deviation from the bimolecular kinetics of the decomposition of α-phenylethyl hydroperoxide in chlorobenzene in the presence of copper stearate as oxidation proceeds may be caused by the formation of complexes of the decomposition products (acetophenone and methylphenylmethanol) and the catalyst. The occurrence of such complex formation has been confirmed qualitatively by a spectrophotometric method. The formation of cobalt(II) and cobalt(III) complexes with α-tetralinone has been postulated to account for the retardation of the decomposition of tetralinyl hydroperoxide in the presence of cobalt 2-ethylhexanoate when α-tetralinone is introduced into the solution[36].

In the oxidation of *o*-xylene in acetic acid in the presence of cobalt acetate the reaction product (*o*-phthalic acid) forms chelate complexes with cobalt(II) and cobalt(III) ions, which alters the oxidation-reduction potential of the system: there is a considerable increase of the stability and hence of the concentration of cobalt(III) in solution. Terephthalic acid, formed in the oxidation of *p*-xylene, also binds cobalt ions into catalytically inactive complexes[103]. A change in the activity of the catalyst as a result of the formation of complexes with acetic and 2-ethylhexanoic acids has been observed in a study of their influence on the decomposition of t-butyl hydroperoxide in the presence of cobalt carboxylates[100]. The changes in the absorption spectrum of cobalt 2-ethylhexanoate in the presence of acids demonstrate qualitatively the formation of complexes of the acid with the cobalt salt. The formation of dinuclear acid–catalyst complexes is possible.

Polar solvents can form complexes with cobalt stearate[34,39]. The rate of decomposition of the hydroperoxide is determined then by the competition between the complex-formation reactions of the catalyst with the hydroperoxide, its decomposition products, and the solvent[39]. A quantitative confirmation of the role of the formation of complexes by copper salts with alcohols, ketones, and acids in the passivation of the catalyst of the decomposition of hydroperoxides was obtained in a study of the decomposition of n-decyl hydroperoxide in the presence of copper stearate in oxygen-containing solvents[102]. Using the method of inhibitors, it was established that there is no chain decomposition of n-decyl hydroperoxide. Alcohols, ketones, and acids inhibit to an equal extent both the decomposition of the hydroperoxide and the formation of free radicals. The relative contributions of the hydroperoxide decomposition pathways do not change in the presence of the compounds used. Furthermore it was shown that under the experimental conditions copper stearate does not oxidise decanol, decanone, and higher carboxylic acids.

Kinetic data for the dependence of the rate of decomposition of n-decyl hydroperoxide on the concentration of alcohols, ketones, or acids and the hydroperoxide established that the observed inhibition of the decomposition of ROOH by the addition of oxygen-containing solvents (S) can be accounted for if it is supposed that, together with the complexes $CuSt_2.2ROOH$, ROOH.S, and $CuSt_2.S$, mixed-ligand complexes $CuSt_2.2ROOH.S$ are produced in the system. The hydroperoxide in such a complex decomposes at rates several orders of magnitude lower than the rate of decomposition of the hydroperoxide in the complex $CuSt_2.2ROOH$. The stabilisation of the hydroperoxide in the complex $CuSt_2.2ROOH.S$ may be due to the fact that in this case the solvent is incorporated in the inner, rather than outer, coordination sphere of the metal. This entails the decomposition of the hydrogen bond between two ROOH molecules bound in a complex with copper stearate and the rate of decomposition of the hydroperoxide falls.

The equilibrium constants for the formation of the complexes $CuSt_2.S$, ROOH.S, and $CuSt_2.2ROOH.S$ were calculated from the kinetic data for the decomposition of the hydroperoxide. At the same time the equilibrium constants for the formation of $CuSt_2.S$ complexes were determined spectrophotometrically from the change in the optical density of $CuSt_2$ solutions in the presence of S.[106] The agreement between the equilibrium constants for the formation of the $CuSt_2.S$ complexes found by the two independent methods made it possible to establish the following mechanism for the decomposition of n-decyl hydroperoxide in the presence of copper stearate and oxygen-containing compounds:

$$CuSt_2 + 2\,ROOH \rightleftarrows CuSt_2 \cdot 2\,ROOH \rightarrow \text{decomposition of ROOH},$$
$$CuSt_2 + S \rightleftarrows CuSt_2 \cdot S,$$
$$ROOH + S \rightleftarrows ROOH \cdot S,$$
$$CuSt_2 \cdot 2\,ROOH + S \rightleftarrows CuSt_2 \cdot 2ROOH \cdot S.$$

VI. DECOMPOSITION OF HYDROPEROXIDES IN THE PRESENCE OF GROUP V–VI METAL COMPOUNDS AND CATALYTIC EPOXIDATION OF OLEFINS BY HYDROPEROXIDES

There has been a recent increase of interest in the study of the mechanism of the catalytic decomposition of hydroperoxides in the presence of Group V–VI metal compounds in connection with the problem of the catalytic epoxidation of olefins by bound oxygen (hydroperoxides, hydrogen peroxide, and peracids) in the presence of molybdenum, vanadium, tungsten, and chromium compounds[107]. The interaction of olefins with hydroperoxides in the presence of these compounds takes place with a high degree of selectivity. Group IB, VII, and VIII transition metals are as a rule relatively inactive in the epoxidation; metals with a constant valence do not catalyse the epoxidation of olefins by hydroperoxides[108,109].

The absence of an appreciable catalytic effect in the epoxidation of olefins in the presence of cobalt, nickel, copper, and manganese compounds, which are typical catalysts of the radical (homolytic) decomposition of hydroperoxide, led to the hypothesis that, in the presence of molybdenum, vanadium, and tungsten compounds, the heterolytic pathway predominates in the decomposition of hydroperoxides[110].

The experimental studies on the decomposition pathways for cumenyl and cyclohexyl hydroperoxides in the presence of vanadium, vanadyl, molybdenyl, and chromium acetylacetonates and stearates showed that the hydroperoxides decompose (as in the presence of transition metals) via two pathways: molecular and free-radical[111]. Depending on the type of catalyst and temperature, the contribution of the radical decomposition may vary from 1 to 100% relative to the overall rate of decomposition of the hydroperoxide[111]. Thus in the decomposition of cumenyl hydroperoxide in the presence of chromium stearate the yield of radicals increases from 1 to 100% as the temperature is raised from 70° to 120°C; cyclohexyl hydroperoxide decomposes in the presence of chromium, vanadyl, and molybdenyl acetylacetonates at 120–130°C with a 3–12% yield of radicals[111].

The study of the kinetics of the decomposition of hydroperoxides in the presence of such catalysts led to the hypothesis that, in contrast to cobalt, copper, and nickel compounds, the molecular decomposition is not in this case a manifestation of the "cage" effect.

The principal decomposition products are acetophenone, dimethylphenylmethanol, α-methylstyrene, and carbon dioxide for cumenyl hydroperoxide and cyclohexanone and cyclohexanol for cyclohexyl hydroperoxide[111]. Phenol, a typical product of the heterolytic decomposition of cumenyl hydroperoxide, is absent from the reaction products, which throws doubt on a significant contribution of the heterolytic hydroperoxide decomposition reaction.

In many studies dealing with the epoxidation of olefins by hydroperoxides it was noted that the epoxidation process is preceded by the interaction of the catalyst with the hydroperoxide, which converts the catalyst into an active valence form. This hypothesis is supported in the first place by the finding that the catalytic epoxidation is always preceded by an induction period, during which the catalyst is altered, in many cases with a change in the colour of the solution. Preliminary incubation of hydroperoxide solutions with the catalyst as a rule eliminates the induction period.

The study of the catalysis of the decomposition of t-butyl hydroperoxide and hydrogen peroxide by vanadium compounds established that a red complex is formed in the initial stage of the process[110-115] when vanadyl chelate complexes are used as the initial forms of the catalyst: vanadyl bis(acetylacetonate) [$VO(acac)_2$]; vanadyl bis-(hexafluoroacetylacetonate) [$VO(hfac)_2$]; vanadyl bis(dipivaloylmethide) [$VO(dpm)_2$]; vanadyl chloride. The $V(acac)_3$ and $V(t\text{-}C_3H_7O)_3$ catalysts do not form a red complex. The stability of the complex depends on the nature of the catalyst employed. It has been suggested[112] that the red colour of the solution is due to the formation of the vanadium(IV)...ROOH complex the decomposition of which involves the transition of vanadium(IV) $\rightarrow$ vanadium(V).

The stoichiometry of the decomposition of H_2O_2 in aqueous solutions in the presence of $VOCl_2$ corresponds to the equation[113]

$$2\,VO^{2+} + H_2O_2 \rightarrow 2\,VO^{+} + 2\,H^{+} + O_2.$$

The formation of the complex $O{=}V{-}OOH^{+}$ in the first stage via the reaction

$$VO^{2+} + H_2O_2 \rightleftarrows O{=}V{-}OOH^{+} + H^{+},$$

with subsequent decomposition of the peroxo-complex via the mechanism

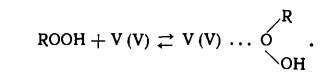
$$O{=}V{-}OOH^{+} \rightarrow VO_2^{+} + OH^{\cdot},$$

$$VO_2^{+} + H_2O_2 \rightarrow VO_3^{+} + H_2O,$$

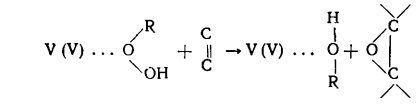
has been postulated.

The VO_3^{+} species can form complexes with free hydroxy-radicals, which ultimately leads to the reduction of vanadium(IV) in the system. The possibility of the interaction of VO_2^{+} with H_2O_2 to form VO_3^{+} has been demonstrated[114]. The disappearance of paramagnetism from the ROOH–$VO(acac)_2$ system suggests that vanadium is in the +5 state in the red complex[111].

The actual nature of the active species in this process has not been established. The virtual independence of the rate of expoxidation of the olefin of the hydroperoxide concentration observed in a kinetic study of the systems allyl alcohol–α-phenylethyl hydroperoxide–vanadium tris-(acetylacetonate)[116], propene–α-phenylethyl hydroperoxide–molybdenum resinate[117], and many others[110,118,119] led to the hypothesis that catalyst–hydroperoxide complexes are formed reversibly:



In this complex there is a possibility of partial polarisation (heterolysis) of the O–O bond[110], which facilitates the subsequent interaction of the hydroperoxide with the olefin:



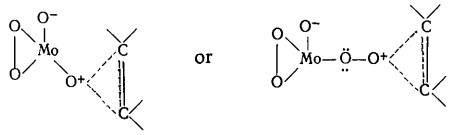
The formation of complexes of t-butyl hydroperoxide with molybdenyl bis(cyclohexanediolate)[120] and molybdenyl bis(acetylacetonate)[121] was observed by NMR from the broadening and partial shift of the signal due to the OH protons of the hydroperoxide in the presence of molybdenum compounds. The existence of two peroxy-species in equilibrium was postulated in this instance[120]:

$$Mo\,(VI)\,ROOH \rightleftarrows Mo\,(V)\,RO_2^{\cdot} + H^{+}. \qquad (13)$$

The formation of the $RO_2^{\cdot}$ radical in the interaction between molybdenum(V) and ROOH has been noted[122].

It has been suggested[123] that molybdenyl peroxo-complexes capable of stoichiometric epoxidation of olefins are formed in the course of the catalytic epoxidation reaction. The capacity of these peroxo-complexes for epoxidation was demonstrated in the epoxidation of olefins[124] and allyl alcohol[125] by the peroxo-complexes $O{=}Mo(O_2)_2L_1L_2$, where L_1 and L_2 are hexamethylphosphoramide and water. Later similar peroxo-complexes [$O{=}Mo(O_2)_2$ and in small amounts $Mo(O_2)_2Cl_2$] were isolated in reactions of organic peroxides with $MoCl_5$ in ethyl alcohol[126].

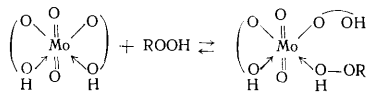
It has been shown with the aid of "labelled" oxygen (^{18}O) that the O=Mo oxo-group is not involved in the epoxidation and that the process proceeds via the formation of intermediate complexes of the type[127]



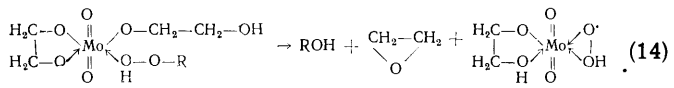
The possibility of the formation of complexes by peroxomolybdenum compounds with an olefin was confirmed[126] by the observation of a change in the colour of $O{=}MoO_4$ from yellow to green in the presence of the olefin. The formation of a complex with allyl alcohol has been demonstrated kinetically for $MoO(O_2)_2L_1L_2$.[125]

Although a peroxomolybdenum(VI) compound has been isolated in the interaction of molybdenum compounds with a hydroperoxide in the absence of an olefin and its capacity for epoxidation has been demonstrated (in stoichiometric proportions of 1 : 1), the mechanism of epoxidation via a successive alternation of stages involving the formation of the peroxo-complex and its reaction with the olefin cannot be regarded as proved. In catalysis by molybdenyl chelate complexes molybdenum bis(diolate) was identified as the main product derived from the catalyst in the presence of an olefin and a hydroperoxide[128,129]. The structure of the diol in the chelate complex corresponds to that of the initial olefin. It has been suggested that such diols can form complexes with hydroperoxides,

probably with dissociation of one of the coordinate bonds between the diol and the molybdenum(VI) ion[120]:

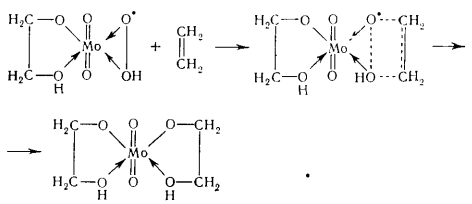


The hydroperoxide in the complex thus formed is activated and can react with the diol in the coordination sphere of the metal to form an oxide (from the diol) and alcohol:



(14)

The initial diolate is reduced and a cyclic catalytic complex is formed via the mechanism



In most investigations of the catalytic epoxidation of olefins the inhibition of the reaction by alcohols was noted. As a rule this effect is attributed to a competitive inhibition mechanism, i.e. the formation of the stable complexes Cat.ROH, which prevent the formation of catalyst–hydroperoxide complexes in the system. Although this mechanism of the inhibition of the epoxidation process by alcohols is extremely probable, it may not be the only one possible.

It has been shown[120] that the introduction of an alcohol into a molybdenum(VI)–ROOH system increases the concentration of the Mo(V).$RO_2^{\cdot}$ species and it has been suggested that the inhibition by alcohols is caused by the acceleration of reaction (13) and the consequent decrease of the concentration of the Mo(VI).ROOH complexes and of the rate of reaction (14). This hypothesis is consistent with the absence of an effect by the alcohol on the kinetics of the formation of the primary red complex in catalysis by vanadyl acetylacetonate and with the increased stability of this complex, if it is supposed that the red complex formed by organic peroxides is analogous to $O{=}VOOH^{+}$. Together with molybdenum(VI) compounds, zero-valent molybdenum carbonyls can serve as active epoxidation catalysts[129–133].

In the absence of an olefin, the hydroperoxide decomposes on $Mo(CO)_6$ via an oxidation-reduction mechanism with a change in the valence of molybdenum. The introduction of phenols into the system leads to the formation of π complexes of the phenol and $Mo(CO)_6$. The decomposition of the hydroperoxide then proceeds without a change in the valence of molybdenum via a synchronous mechanism and involves a reaction between the phenol in the complex and two hydroperoxide molecules[134].

The study of the infrared spectra of molybdenum hexacarbonyl in the presence of an olefin and a hydroperoxide showed that the valence state of molybdenum does not change in the epoxidation reaction[130–133]. The kinetic epoxidation curves nevertheless show a distinct induction period, which suggests the necessity for an $Mo(CO)_6$ dissociation stage. An NMR study of the $Mo(CO)_6$–α-phenylethyl hydroperoxide system in dichloroethane demonstrated the formation of the outer-sphere complexes $Mo(CO)_6$.ROOH with subsequent displacement of CO and the incorporation of the hydroperoxide in the inner coordination sphere:

$$Mo(CO)_6 + ROOH \rightarrow Mo(CO)_6 \cdot ROOH \xrightarrow{-CO} Mo(CO)_5 \cdot ROOH.$$

It is suggested that the epoxidation proceeds via a stage involving the formation of the mixed-ligand complexes $Mo(CO)_{6-1-n}.(olefin)_n.ROOH$.

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Short-lived Phenoxy- and Semiquinone Radicals

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The results of the principal studies of the absorption spectra and the kinetics of the destruction of short-lived phenoxy- and semiquinone radicals in the liquid phase are examined. A systematic account is given of the results of investigations of their interaction with metal compounds. Much attention is devoted to the photochemical method of generating phenoxy- and semiquinone radicals from phenolic and quinonoid compounds.
The bibliography includes 205 references.

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I. INTRODUCTION

In the vast majority of cases the reactions of phenolic compounds in chemical and biological processes have free-radical mechanisms. The phenoxy- and semiquinone radicals formed under these conditions as intermediates and the related flavosemiquinone radicals are π radicals and belong to the class of aromatic radicals. The study of the characteristics of phenoxy-radicals is an important task in connection with the extensive use of phenols as inhibitor-stabilisers in various branches of theoretical and applied chemistry[1-3] and recently also in experimental biology and medicine[4]. There has been an immense growth of interest in the last decade and a half in this field of research in connection with studies by Emanuel' and his coworkers[4-11].

A number of monographs and reviews are devoted to stable phenoxy- and semiquinone radicals[3,12-16]. As a result of the development of pulse methods, extensive data on the physicochemical properties of short-lived phenoxy- and semiquinone radicals have accumulated during the last 10–15 years.

It is therefore desirable to survey the available literature data for the fundamental reactions of phenoxy- and semiquinone radicals and their physicochemical properties.

II. METHODS FOR THE INVESTIGATION OF THE PHYSICOCHEMICAL PROPERTIES OF SHORT-LIVED RADICALS

Almost all the techniques for the investigation of reactivity can be applied to phenoxy- and semiquinone radicals. In this review the term "unstable" or "short-lived" is applied to a radical whose lifetime is shorter than one second in the absence of oxygen at room temperature in a non-viscous solvent at concentrations in the range 10^{-7} to 10^{-5} M.

For a time the ESR method (in its usual version) was the main procedure for the investigation of the properties of radicals. Its use in the study of short-lived radicals is extremely difficult. In such cases one employs a flow system or the radical precursor is irradiated directly in the cavity of the spectrometer. In certain cases the radicals can be stabilised owing to the characteristics of the solvent—a highly alkaline medium (in the case of semiquinone radicals) or the formation of a complex with the solvent[13]. The method of low-temperature stabilisation[17], in which the radicals are stabilised in a solid matrix and their spectra are recorded, has been widely used. In recent years the absorption spectra of aromatic and other radicals, stabilised in a solid poly(methyl methacrylate) (PMMA) or adamantane matrix, have been recorded at room temperature[18-20].

Pulse methods (flash photolysis and pulse radiolysis) have a considerable scope in the study of the properties of short-lived radicals. The use of flash photolysis with detection of intermediates from their ESR spectra is extremely promising.

The absorption of light by an aromatic molecule, for example phenol, leads to the formation of an unstable excited state, which is deactivated either as a result of a photophysical process, for example fluorescence or phosphorescence, or photochemically, i.e. via dissociation into radicals or ionisation. The radicals or radical-ions thus formed can be detected, for example, from their absorption spectra. The method of pulse radiolysis has been also widely used to study aromatic radicals; it differs from flash photolysis by the fact that the excitation is achieved by a short pulse of high-energy electrons†.

† In order to obtain high non-equilibrium concentrations of phenoxy- and semiquinone radicals, water was subjected to pulse radiolysis in the presence of the initial phenolic or quinonoid compound. The aqueous solutions contained 0.1–10% of organic additives (alcohol, acetone, formate, etc.) and could be saturated with N_2O to remove undesirable water radiolysis products from the reaction mixture. All the experiments were performed at room temperature.

III. THE INVOLVEMENT OF PHENOXY- AND SEMIQUINONE RADICALS IN CHEMICAL AND BIOLOGICAL PROCESSES IN THE DARK

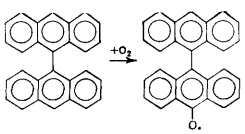
1. Phenoxy-radicals

Phenoxy-radicals are intermediates in various reactions where phenol is oxidised—by inorganic oxidants, oxygen, alkoxy- and peroxy-radicals, oxidation enzymes, anodically, etc. They are formed in hydrocarbon oxidation reactions inhibited by phenol. The mechanism of the action of phenolic inhibitors in free-radical reactions reduces to chain termination owing to the interaction of the phenol (RhOH) with the chain-propagating radicals R$^{\cdot}$ or RO$_2^{\cdot}$:[1]

$$R^{\cdot}\,(RO_2^{\cdot}) + PhOH \rightarrow RH\,(ROOH) + Ph\dot{O}.$$

Aromatic radicals RO$^{\cdot}$ are as a rule incapable of propagating the chain process further and are destroyed by interacting with one another or with the chain-propagating radicals[1,2,21].

Aryloxy-radicals are also formed when condensed aromatic compounds without OH groups are oxidised by oxygen. The oxidation of anthracene leads to the formation of the corresponding aryloxy-radical[22], while the oxidation of bianthryl proceeds via the substitution of its most reactive hydrogen atom by oxygen[23]:



Phenolic compounds are extremely widely distributed in nature. It has been suggested that phenolic substances are involved in the growth, development, immunity, resistance to cold and harmful radiation, respiration, and photosynthesis in plants, i.e. in almost all their vital processes[24,25]. It has been established that certain biologically important phenolic substances are capable of reversible oxidation with formation of the corresponding phenoxy-radicals as intermediates and it has been suggested that these properties constitute the basis of the pharmacological activity of such compounds[25]. Phenolic compounds are incapable of participating in various enzymatic and photochemical oxidation-reduction processes which are of great biological importance[25]. It is nowadays regarded as proved that oxidative coupling of phenols is one of the principal stages in the biosynthesis of natural products[26].

2. Semiquinone Radicals

o- and *p*-Hydroxyphenoxy-radicals and their anions as well as their derivatives constitute the group of semiquinone radicals. As early as the 1930s, Michaelis and coworkers[27] showed that the two-electron oxidation of hydroquinone or the reduction of quinone proceeds via a stage involving the formation of an intermediate containing an odd number of electrons—a semiquinone radical. The existence of semiquinone radicals in quinone reduction or hydroquinone oxidation processes was demonstrated for the first time in measurements of magnetic susceptibility and in potentiometric measurements[27]. *o*- and *p*-Benzosemiquinone radical-anions are relatively stable in an alkaline medium, which makes it possible to record their intense ESR signals in aqueous or alcoholic media at room temperature[28,29].

Like phenoxy-radicals, semiquinone radicals are the primary products of the oxidation of various hydroquinones by inorganic oxidants, by atmospheric oxygen, by enzymes[30], etc. They can probably be formed also in the catalytic oxidation of phenol by oxygen, as shown by the formation of hydroquinone and catechol as the final products of such a reaction[31]. Quinones are well known in organic chemistry as electron acceptors which are reduced to dihydroquinone via the intermediate formation of a semiquinone radical.

A wide variety of numerous quinonoid compounds are encountered in nature and are involved in oxidation-reduction reactions[32,33]. Semiquinone radicals play an important role in biological systems as active agents in electron transfer reactions in living organisms, plants, and microorganisms[34,35]. The simplest quinones (*p*-benzoquinone, chloranil, duroquinone, and naphthoquinone) have aroused interest, because they can be regarded as models for more complex quinones—coenzyme Q, vitamins K, plastoquinones, flavin-adenine dinucleotide, etc. Studies on reversible oxidation reduction reactions of riboflavin (vitamin B$_2$), which also proceed via the formation of flavosemiquinone radicals, are of great interest from the biological point of view.

IV. FUNDAMENTAL PHOTOCHEMICAL PROCESSES OCCURRING ON PHOTOEXCITATION OF PHENOLS AND QUINONES

1. Photolysis of Phenols

The majority of the reactions leading to the formation of phenoxy-radicals are associated with the abstraction of hydrogen from the hydroxy-group of phenol under the influence of oxidising agents. The dissociation of the O–H bonds in phenols (as well as PhO–CH$_3$, PhO–C$_2$H$_5$, and PhO–COR bonds) with formation of phenoxy-radicals can occur also under the influence of ionising and ultraviolet radiation or ultrasonic waves[36–56]. The simplest phenols are photolysed in the gas phase via the reaction[45]

$$PhOH + h\nu \rightarrow PhO^{\cdot} + H^{\cdot}.$$

An energy diagram has been plotted for this decomposition pathway of the phenol molecule[45], according to which the absorption of a photon by the phenol results in its transition from the ground state to the first singlet excited state $^1\pi_1$. This level intersects the dissociative level $^3\sigma_0$, and the system can pass to the $^3\sigma_0$ state, which entails the dissociation of the O–H bond and the formation of the radicals PhO$^{\cdot}$ and hydrogen atoms H$^{\cdot}$.

In the pulse photolysis of phenoxide ions in the liquid phase a phenoxy-radical is formed, as in the photolysis of phenol, which indicates the photoionisation of the anion via the reaction[54,55]

$$PhO^- + h\nu \rightarrow PhO^{\cdot} + e^-_{hydr.}$$

The photoionisation of phenols and their anions in a solid matrix at low temperatures proceeds via a two-photon pathway with participation of the triplet excited state[56–62]. The nature of this process in liquid media, particularly in polar liquids, is less clear. The earlier attempts to observe a non-linear relation between the initial yield of solvated electrons, obtained in the photolysis of *p*-cresol, and light intensity were unsuccessful[50].

It was suggested[64] that in certain cases a one-photon process may proceed via an intermediate semi-ionised state, which is produced directly from the unrelaxed excited singlet state. As a result of the energy gain on solvation, photoionisation can be induced by light the energy of whose quanta is less by 3–4 eV than the ionisation potential in the gas phase[65]. It has been shown[18] that the corresponding naphthoxy-radicals are formed from the molecules of α- and β-naphthols in the excited singlet state in a PMMA matrix.

In the liquid-phase photoexcitation of phenols, phenoxy-radicals are formed via the reactions[51,66,67]

$$\mathrm{PhOH} + h\nu \rightarrow \mathrm{PhOH}^* \begin{cases} \xrightarrow[-\mathrm{H}^+]{(a)} (\mathrm{PhO}^-)^* \rightarrow [\mathrm{PhO}^\cdot + e_{solv}] \rightarrow \mathrm{PhO}^\cdot + e_{solv} \\ \xrightarrow{(b)} [\mathrm{PhO}^\cdot + \mathrm{H}^\cdot] \rightarrow \mathrm{PhO}^\cdot + \mathrm{H}^\cdot \end{cases} , \quad (1)$$

where the solvent "cage" is represented by square brackets.

In the flash photolysis of phenol and cresols the relative yield of hydrated electrons falls when the pH becomes less than the pK of the corresponding unexcited phenol molecule[50]. After the dissociation of the phenol molecule in the singlet excited state (pathway a), the electron is "ejected" with formation of a phenoxy-radical. Subsequent studies confirmed that the pK of phenol and cresols in the first singlet state are smaller by 5–6 units than in the ground state[68,69]. The relative contributions of the decomposition pathways of the excited phenol molecule, a or b, are independent of many factors, primarily temperature, solution pH, and the polarity of the medium[51,66]. A detailed mechanism of the photoionisation of aromatic molecules in liquids has been discussed[64,70].

According to Feitelson and Hayon[51], more than 70% of the radicals generated from phenols are obtained via photoionisation (pH 7.0; 25°C) and the remainder via the dissociation of the O–H bonds. (The quantum yield in the dissociation of the O–H bond amounts to about 0.01 for various media[53].) On the other hand, the photoionisation is much less effective with the phenol than that with the corresponding anion[71]. The photoionisation of phenols and their anions in alkaline media proceeds via two-photon and one-photon processes respectively[65]. The concentration of phenoxy-radicals formed under the influence of the flash is proportional to the light intensity I^n, where n varies from 2 to 1 over a relatively narrow pH range. Absorption due to phenoxy-radicals is observed in air-saturated solutions, the radicals being formed in a somewhat lower yield and $n = 1.5$.

Studies of the photolysis of aqueous solutions of phenols in the absence of oxygen (at 25°C) with added hexa-2,4-diene, a typical quenching agent for the triplet state, showed that in the photolysis of many phenols the electron is also ejected from a long-lived excited state, possibly the triplet state[51].

Either halogenophenoxy-radicals or hydroxyphenyl radicals may be formed in the photolysis of halogenophenols. The photolysis of iodophenols results in the formation of hydroxyphenyl radicals[18,146], as in the photolysis of p-chlorophenol and monobromophenols[48,73].

The photolysis of 2,4-dibromophenol and 2,4,6-tribromophenol yields the corresponding phenoxy-radicals[72,45]. The absorption recorded in the flash photolysis of certain chlorophenols is due to the formation of chlorophenoxy-radicals[45].

2. Photochemical Reactions Leading to the Formation of Semiquinones

Semiquinone radicals may be obtained by the photochemical oxidation of the corresponding hydroquinones or by the photochemical reduction of quinones. The photochemical oxidation of hydroquinones proceeds partly in the same way as the photolysis of phenols [see Eqn. (1)]. Thus the formation of the corresponding semiquinone radicals and hydrated electrons was observed in the flash photolysis of hydroquinone and catechol in water[59].

The photochemistry of quinones has been vigorously investigated in connection with the elucidation at the molecular level of the destructive effect of light on certain biological objects[33] and also the possible initiation of electron transfer in biological systems following the absorption of light by a quinone[74]. It has been shown that certain alkylquinones are bound to chlorophyll in leaf chloroplasts[33,34]. It has been suggested, that, apart from their function as acceptors in the electron-transport chain, these quinones can play a definite role in photophosphorylation[75].

The damaging influence of ultraviolet light on living organisms is associated with photochemical reactions of quinones, which are the most likely targets for radiation[76]. Semiquinone radicals are frequently the primary products of the photochemical excitation reactions of quinones under these conditions[76–78].

The photochemical reduction processes involving quinones have been studied in fair detail. In an excited state quinone molecules abstract a hydrogen atom (or electron) from the solvent molecule or from another hydrogen (or electron) donor present in solution with formation of a semiquinone radical. Depending on the pH, an acid–base equilibrium involving the half-reduced forms of quinones is then rapidly established. The problem arises as to the nature of this excited state of the quinone. Studies on the kinetics of the destruction of the triplet state of duroquinone DQ(T) and the semiquinone radical DQH$^\cdot$ in liquid paraffin[79,80] showed that DQH$^\cdot$ is formed mainly via the reaction

$$\mathrm{DQ}(\mathrm{S}^*) + \mathrm{RH} \rightarrow \mathrm{DQH}^\cdot + \mathrm{R}^\cdot .$$

However, experiments on energy transfer established that DQH$^\cdot$ is formed also by a path involving the triplet state[81]. It was subsequently shown by laser photolysis that the durosemiquinone radical is indeed formed from the triplet state in ethanol[82].

The fact that DQ(T) is destroyed in liquid paraffin, giving rise to DQH$^\cdot$, has not been rigorously demonstrated[82]. Studies of the photochemical reduction of chloranil have also demonstrated that the photoexcited triplet state of chloranil is quenched by ethanol with direct formation of a semiquinone radical-anion[83]. The lifetime of the triplet state of p-benzoquinone in ethanol is 10 ns and therefore the rate constant for the abstraction of a hydrogen atom from the solvent $k > 10^8$ s^{-1}.[83,84]

The mechanism of the photochemical reduction of p-benzoquinone in ethanol at low temperatures has been considered[85,86]. The photochemical reduction of 1,4-naphthoquinone proceeds with the intermediate formation of the neutral naphthosemiquinone radical[87].

In certain cases the formation of semiquinone radicals on photochemical reduction of quinones is accompanied by electronic polarisation[84,87]. Immediately after the flash, an emission signal appears in the ESR spectrum, is converted into an absorption signal, and then diminishes owing to the destruction of the radicals[84,87].

The pK values of semiquinone radicals in water are fairly well known (Table 2). The assignment of the observed absorption in an organic solvent to a neutral semiquinone radical or radical-anion is usually based on an analysis of ESR spectra [87,88], but here too certain difficulties arise. The photoexcitation of chloranil in ethanol or methanol leads to the formation of the chloranil radical-anion [88], while in another study [89] it is suggested that the primary product of such photochemical reduction in isopropyl alcohol (or dioxan) is a nuetral radical.

The photochemical reduction of anthraquinone derivatives in alcoholic media has been studied in greatest detail, since this process simulates the photochemical degradation of cellulose sensitised by anthraquinone dyes and is of great practical importance [90-96].

Anthraquinone derivatives are reduced photochemically in alcoholic solutions via the reaction

$$AQ\,(T) + RCH_2OH \rightarrow AQH^{\cdot} + R\dot{C}HOH$$

and in alkaline media via the reaction

$$AQ\,(T) + OH^{-} \rightarrow AQ^{\cdot-} + OH^{\cdot}.$$

The resulting semiquinone radical-anion is fairly stable in alkaline solution in the absence of oxygen.

The quinones involved in photochemical biological processes (plastoquinones, tocoquinones, and α-tocopheryl-quinones) also give rise to the corresponding semiquinone radicals on photoexcitation. The final photochemical reduction products from certain plastoquinones and tocoquinones are o-quinone methides [76-78]. The photochemical reduction of many quinones with ring substituents proceeds via an intramolecular mechanism [97-99].

The triplet state responsible for the formation of the semiquinone radical from 1,4-benzoquinone, 1,4-naphthoquinone, and anthraquinone is probably of the $n-\pi$ type [100-103], while the triplet states of duroquinone and chloranil are of the $\pi-\pi^*$ type [82,101,104]. The precursor of the radical is probably the lowest triplet state of the corresponding quinone in all cases where semiquinones are formed [63,87].

The formation of flavosemiquinone radicals, particularly those derived from riboflavin, has been observed in the photochemical reduction of flavins or in their reduction by electrons [105-108,110-115].

It was initially suggested that dihydroriboflavin is formed via the abstraction of two hydrogen atoms from the water molecule [116-118]. Objections were raised to this mechanism [119] on the basis of the process energetics and it was postulated that the decolorisation of riboflavin proceeds via the photochemical oxidation of its own ribityl chain. There is evidence for an intramolecular decolorisation mechanism, obtained in a series of kinetic and polarographic studies by pulse photolysis and theoretical calculations [108,109,120-127]. It has been shown that the lowest long-lived triplet state is photochemically reactive in the anaerobic photochemical decolorisation of riboflavin and flavin mononucleotide [107-110,119]

It has been shown [109,127] that the singlet state of riboflavin can also be involved in photochemical reduction and that this pathway is probably the only one giving rise to the formation of the flavosemiquinone radical in air-saturated solutions.

V. SENSITISED PHOTOCHEMICAL OXIDATION OF PHENOLS AND PHOTOCHEMICAL REDUCTION OF QUINONES

In a study of the photochemical oxidation of a number of sterically hindered phenols by molecular oxygen it was observed that, on irradiation without a sensitiser, the initial phenols remain unchanged [128]. Sensitised photochemical oxidation of sterically hindered phenols proceeds via the following mechanism: a complex is formed by the excited molecule of the sensitiser and oxygen and abstracts the hydrogen atom from the hydroxy-group of the phenol with formation of the phenoxy-radical [128]. (In the photochemical oxidation of unsubstituted phenol and cresol under the influence of light with $\lambda = 253.7$ nm, it was established [73] that the presence of oxygen or other oxidants is not essential for the formation of the phenoxy-radical.)

According to another mechanism of the sensitised photochemical oxidation of phenols [129-135], the phenol is attacked by an excited sensitiser molecule, which leads to the abstraction of the hydrogen atom from the phenolic hydroxyl or to the loss of an electron by the phenoxide ion. Reactions proceeding via this mechanism have been observed [130-136] in the sensitised photochemical oxidation of phenol and its derivatives by eosin (E) and related dyes.

The photochemical oxidation reactions sensitised by eosin are of great interest for photobiology, since it has been shown that eosin causes photodynamic inactivation of proteins [136]. The experiments performed by flash photolysis (kinetic and spectrophotometric) have shown that the attack on phenol by a dye molecule in the triplet state results in the formation of a phenoxy-radical and a semiquinone radical derived from the dye [136]:

$$E\,(T) + PhOH \rightarrow EH^{\cdot} + PhO^{\cdot}.$$

It has been established that excited states of 9,10-anthraquinone-2-sulphonic, 9,10-anthraquinone-2,6-disulphonic, and 9,10-anthraquinone-2,7-disulphonic acids are quenched chemically by phenol and hydroquinone with formation of the corresponding phenoxy- (p-benzosemiquinone) and anthrasemiquinone radicals [72,90]. Various α-diketones in an excited state are also capable of oxidising phenols with formation of ketyl and phenoxy-radicals [137,138]. In the quenching of the luminescence of diacetyl by phenols there is a reversible abstraction of a hydrogen atom with formation of phenoxy-radicals [139].

Certain dyes and pigments in an excited state are capable of reducing quinones to semiquinone radicals. Thus the following reaction takes place in the photoexcitation of chlorophyll in alcohols in the presence of p-benzoquinone (duroquinone, vitamin K, and α-tocopheryl-quinone) [132,140-143]:

$$Chl^{*} + Q \rightarrow Chl^{+} + Q^{\cdot-}, \qquad (2)$$

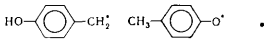
where Chl* is the excited chlorophyll molecule (most probably in the triplet state) and $Q^{\cdot-}$ the semiquinone radical. Eosin in the excited triplet state reduces p-benzoquinone via a type (2) reaction, being oxidised itself to a radical-cation [144].

VI. ABSORPTION SPECTRA AND ACID–BASE PROPERTIES OF PHENOXY- AND SEMIQUINONE RADICALS

The absorption spectra of a number of phenoxy- and semiquinone radicals were recorded in the flash photolysis and pulse radiolysis of phenolic and quinonoid compounds.

The problem of the assignment of the observed absorption in the flash photolysis of aromatic compounds to any specific structural formula is solved individually in most cases[42,43]. Either the triplet state of the molecule or a radical are responsible for the absorption. This problem can be solved by an additional study of the kinetics of the reaction with oxygen, the application of the method of $T-T$ energy transfer, the study of the interaction of the intermediates with various additives, a comparison of the absorption spectra in the liquid and solid phases, etc. Investigation of the dependence of the absorption on the polarity of the medium, pH, ionic strength, and other parameters makes it possible to determine the charge on the transient species.

A study of substituted phenols by flash photolysis showed that, in principle, different radicals can be formed. For example, benzyl and phenoxy-radicals may be formed in the photolysis of *p*-cresol:



In such cases one has to decide to which radical the observed spectrum should be assigned. The spectra of benzyl and phenoxy-radicals differ appreciably in the shape of the bands and in the relative intensities of the long-wavelength and short-wavelength transitions. Flash photolysis of *p*-cresol yielded a spectrum almost identical in form and intensity to that of the phenoxy-radical. On this basis, it was concluded that the primary photochemical process is the formation of a *p*-methylphenoxy-radical[42].

In general the identification of the spectra of aromatic radicals has been based on the study of a series of related substituted compounds[43,145]: the method is particularly convenient and reliable for aromatic compounds, since there are many such compounds and in most cases there is a possibility of cross checks.

1. Phenoxy-radicals

The spectra of phenoxy-radicals are characterised by a system of bands in the region of 300 and 400 nm.[42] The absorption spectrum of the unsubstituted phenoxy-radical was recorded for the first time in the flash photolysis of phenol and anisole vapours in the gas phase[36]. The spectrum consists of a single diffuse band with a maximum at 292 nm. The long-wavelength band in the region of 400 nm has been observed[37,38] in the flash photolysis of phenol in various solvents. Low-temperature studies confirmed the validity of the band assignment[40,42].

The formation of phenoxy-radicals has also been established[44] in the photolysis of phenol, anisole and phenetole in a nitrogen matrix at 4.2 K. In addition to the earlier data[40], bands were found at 295 and 396.5 nm together with a broad band at 240 nm, which correspond to the absorption by the phenoxy-radical. Further photolysis by light in the wavelength range 225–345 nm led to the degradation of the phenoxy-radical itself. Subsequently, a long-wavelength band system with maxima at 395 and 382 nm was observed in the flash photolysis of phenol vapour in the presence of argon[42,46].

The absorption spectra of eighteen different alkylphenoxy-radicals were obtained by Land and Porter in the flash photolysis of the corresponding phenols[45]. They showed that aliphatic substituents have an insignificant influence on the absorption spectrum of the phenoxy-radical, leading to slight shifts of the long-wavelength band system as a function of the position of the substituent in the ring. Phenoxy-radicals are the principal short-lived species detected in the flash photolysis of proteins such as egg albumin, where they are formed from compounds of the type of tyrosine[145].

Phenoxy-radicals with large alkyl substituents have spectra in which the band distribution remains largely the same as in the spectrum of the unsubstituted phenoxy-radical, their intense colour being due to broad bands extending to the visible region. Alkylated phenoxy-radicals are blue and alkoxy- and phenyl groups cause a hypsochromic shift in the visible region, giving rise to radicals with $\lambda_{max} \simeq 530$ nm. On the other hand, electron-accepting substituents (formyl, keto-, and cyano-groups) cause a bathochromic shift and the radicals can be blue or green[12]. A weak diffuse absorption is observed in the region of 600 nm in the spectra of certain trialkylphenoxy-radicals[48]. The existence of such a broad band was also expected for the unsubstituted phenoxy-radical[42]; it was observed in the gas phase under conditions of high resolution[46]. Apart from the 380 and 395 nm bands, which correspond to $\pi-\pi^*$ absorption like the 292 nm band, a broad and weak absorption band was detected in the range 530–610 nm with $\lambda_{max} = 600$ nm; it is probably due to absorption of the $n-\pi^*$ type[43,46].

Studies on the absorption spectra of phenoxy-radicals in PMMA showed that the long-wavelength absorption limit of the radical is 850 nm.[18] However, on the basis of quantum-chemical calculations, the author[18] believes that the long-wavelength absorption in the spectrum of the phenoxy-radical in the region of 600 nm is also of the $\pi-\pi^*$ type. The theory of the absorption spectra of the simplest aromatic radical has been discussed[42].

The absorption spectra of phenoxy-radicals have been recorded in the pulse radiolysis of phenol and *p*-cresol in water[49]. The extinction coefficients of phenoxy-radicals were determined either by pulse radiolysis (when the radiation yields of the radiolysis products are known)[49] or by comparison with the absorption of hydrated electrons formed in the photolysis of phenoxide ions. When the latter method was used, unduly high extinction coefficients were apparently obtained in many instances. This is probably because the hydrated electron has a very short lifetime, comparable to the duration of the flash. A comparatively simple and reliable method for the determination of the extinction coefficient of phenoxy-radicals in experiments on the photochemical oxidation of phenols sensitised by anthraquinone-2,6-disulphonic acid has been proposed[72]. When this method is used, it is possible to obtain the extinction coefficients of halogenophenoxy-radicals[72,146]. (Halogenophenols do not give rise to hydrated electrons on photochemical excitation or effectively quench such electrons[66].) Data for the spectra of the simplest phenoxy-radicals are listed in Table 1.

The differences between the spectra of the radicals at different temperatures and in different solvents are usually small. Small changes in the absorption maxima and shapes of the bands are observed in gas–liquid–solid transitions[42].

In solutions, over the entire range of acidities (up to solutions containing 12 M H_2SO_4), phenoxy-radicals are present as uncharged species[40,43]. Protonation of the radicals usually alters greatly the absorption spectrum and such changes can be readily detected. The protonated phenoxy-radical $PhO\mathring{H}^+$ is a very powerful acid and cannot be observed with appreciable equilibrium concentrations[40,43]. The pK of certain substituted phenoxy-radicals have been obtained by flash photolysis and all the pK values are less than -1.[43]

Quantum-chemical calculations[147] showed that the existence of unsubstituted phenoxy- and semiquinone radical-cations in an aqueous medium is virtually impossible.

Table 1. The absorption maxima and extinction coefficients of phenoxy-radicals in water at 20°C.

Radical	λ_{max}, nm	ε, litre mole^{-1} s^{-1}	References
Phenoxy-	402	1 800*	42
	299	5 000	42
	400±5	2200±200	49
	290±5	4000±800	49
	399	11 000	50
	400	2 300	72
o-Methylphenoxy-	395, 380, 363	—	45
	395	8 700	50
	405	3 400	72
m-Methylphenoxy-	412, 381, 372	—	45
	412	4 800	50
	420	3 000	72
p-Methylphenoxy-	405, 385, 368	—	45
	388, 405	—	54
	405	15 000	50
	405±5	2400±400	49
	295±5	5000±1000	49
	410	3200±300	51
	400	2 500	72
m-Nitrophenoxy-	450	490	72
2,4-Dibromophenoxy-	420	3 700	72
Phenoxy-radical from tyrosine	410	2 100	72
	410	2750±200	51
p-Iodophenoxy-	420	2 800	146

*In hexane.

2. The Absorption Spectra and Dissociation Constants of Semiquinone Radicals

The absorption spectra of many short-lived *p*-semiquinone radicals have been recorded by methods of flash photolysis[79,80,147–153] and pulse radiolysis[74,154–166] in studies on hydroquinone and quinones. Pulse radiolysis proved to be a convenient method for the investigation of the properties of semiquinone radicals (the studies were performed mainly in aqueous solutions). When this method is used to generate the radicals, there is no need for the formation of an excited state (which may be readily quenched by impurities or oxygen) and it is possible to determine the extinction coefficients. The study of the dependence of the absorption intensity of the radical on the pH of the solution under otherwise constant conditions makes it possible to obtain "titration curves" of the radicals and to determine the pK values, which for the majority of *p*-semiquinone radicals are in the range 3–6 (Table 2).

The spectra of the majority of semiquinone radical-anions have maxima in the range 400–450 nm (Table 2), while the absorption maxima of the neutral radicals are displaced to the ultraviolet and are located in the range 370–425 nm.[163] This is consistent with the general postulate that the basic forms of free radicals absorb at lower energies than the acid forms[163]. In most cases semiquinone radicals and radical-anions have absorption bands in the ultraviolet and far ultraviolet[165,166] but, with one exception[167], these bands have not been investigated in detail.

The electron combined with an excited quinone molecule converts its quinonoid structure into an aromatic structure and the absorption of light involves transitions of the $\pi-\pi^*$ type in semiquinone radicals[125].

The absorption spectrum of the *p*-benzosemiquinone radical-anion has been investigated thoroughly[167]. The radical-anion was obtained by oxidising hydroquinone with manganese dioxide and its absorption and ESR spectra were recorded; the latter made it possible to determine the concentration of the radical-anions. The results are in Table 2. The absorption spectra of a number of semiquinone and flavosemiquinone radicals have also been published[70,105,106,110,164–166,170,171]. The flavosemiquinone radicals investigated differ only by the substituents in the isoalloxazine ring and have very similar absorption spectra.

Table 2. The absorption maxima, extinction coefficients, and dissociation constants of semiquinone radicals in aqueous, aqueous organic, and organic media at 20°C.

Initial quinone	$Q^{\cdot-}$		$QH^{\cdot}$			References
	λ_{max}, nm	ε, litre mole^{-1} cm^{-1}	λ, nm	ε, litre mole^{-1} cm^{-1}	pK	
p-Benzoquinone	430	6 100	410	4 300	4.1	164[a]
	425	7 300	415	5 500	4.0	154
	430	5 400	—	—	—	167
	404	4 600	—	—	—	167
	371	3 700	—	—	—	167
	316	40 000	—	—	—	167
	310	33 000	—	—	—	167
	425	7 200	415	4 500	4.0	163[b]
Duroquinone	445	—	430	—	5.1	158[c]
	445	7 100	425	4 000	5.1	163[b]
	—	—	410	3 500	—	168[e]
1,4-Naphthoquinone	390	—	380	—	4.1	158[c]
	390	12 500	370	7 100	4.1	164[a]
	390	13 000	370	7 300	4.1	163
Vitamin K_3	400	10 200	380	9 900	5.5	164[c]
	395	12 000	370	9 500	4.5	165
	300	12 500	290	6 000	—	165
9,10-Anthraquinone	395	7 800	375	11 000	5.3	163[d]
	480	7 300	—	—	—	163
9,10-Anthraquinone-1-sulphonic acid	400	8 000	385	12 000	5.4	74
	500	8 000	—	—	—	74
9,10-Anthraquinone-2-sulphonic acid	500	8 200	—	—	3.25	74
	398	9 800	387	14 000	3.9	166
	465	8 000	—	—	—	166
	496	9 500	—	—	—	166
9,10-Anthraquinone-2,6-disulphonic acid	395	—	390	—	3.2	158[c]
	525	—	—	—	—	158[c]
	520	8 000	—	—	2.3	153
Riboflavin	560[f]	170	560	5 130	8.3	105
Flavin mononucleotide	—	—	560	3 050	—	106
9,10-Phenthrenequinone-3-sulphonate	—	—	485; 525	—	7.5	169
Chloranil[g]	—	—	420	7 300	—	89
	—	—	435	7 700	—	89
	—	—	448	6 000	—	89

The compositions of the aqueous solutions were as follows: *a*) 1 M isopropyl alcohol and 1 M acetone; *b*) 1–2 M t-butyl alcohol; *c*) 5 M isopropyl alcohol and 2 M acetone; *d*) 3 M isopropyl alcohol; *e*) solution in cyclohexane; *f*) not absorption maximum; *g*) solution in dioxan. In the remaining cases the solvent was water.

Certain neutral semiquinone radicals are capable of combining with an H^+ ion and of being converted into an acid form:

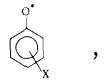
$$QH \overset{H^+}{\rightleftarrows} QH_2^+.$$

Thus, Land and Porter [148] and Land and Swallow [105] showed that the pK values for this type of equilibrium involving the durosemiquinone and flavosemiquinone radicals are respectively −1.1 and 2.3.

VII. KINETICS OF THE DESTRUCTION OF RADICALS

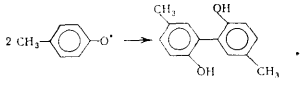
1. Phenoxy-radicals

Dimerisation is one of the most important reactions in the chemistry of phenoxy-radicals. It constitutes the basis of the oxidative coupling of phenols and leads to the formation of C−C, C−O, and O−O bonds [25]. Dimerisation involving the C−C and C−O bonds proceeds exclusively in the *ortho*- and *para*-positions with respect to the phenoxy-oxygen [26]. For example, *p*-cresol oxidised under different conditions by potassium hexacyanoferrate(III) in an alkaline solution gives rise to different final products: the *o*-dimer (2,2′-dihydroxy-5,5′-dimethylbiphenyl), the trimer, pummerer's ketone, and polymers [26]. The formation of more complex products can be account for by further interaction of the dimers with phenoxy-radicals or by the isomerisation of the dimers. The kinetics of the destruction of the *p*-methylphenoxy-radical, obtained in the pulse photolysis of *p*-cresol, have been investigated in detail [50]. It was found that the reaction obeys second-order kinetics, i.e. the radicals disappear by dimerisation. The experimental values of k/ϵ remain constant within the limits of the error over a wide range of concentrations of the initial *p*-cresol [50]. The rate constants and the values of k/ϵ are listed in Table 3, which includes data for phenoxy-radicals of the type



where X are various substituents.

The main product of the dimerisation of the *p*-methylphenoxy-radical in aqueous solution saturated with nitrogen is the *o*-dimer:



The dimerisation of two unsubstituted phenoxy-radicals results in the formation of a much greater number of products (about ten). [26] In the dimerisation of two α-naphthoxy-radicals almost all the possible products of *ortho*- and *para*-coupling are obtained and there are none containing the C−O bond; β-naphthoxy-radicals are destroyed with formation of binaphthols containing mainly the $C_{(1)}-C_{(1)}$ bond and to a much smaller extent the $O-C_{(1)}$ bond [174].

The absolute values of the rate constants for the destruction of phenoxy-radicals naturally depend markedly on the extinction coefficient adopted and are on average smaller than the k_{diff} calculated from the Debye formula [45,51,72,137]. The unduly high values of the constants frequently obtained by the Debye formula [175] can be partly accounted for by the lack of rigour in the assumptions made in its derivation.

A relation has been established [72] between the structure and the rate constant for the recombination of phenoxy-radicals.

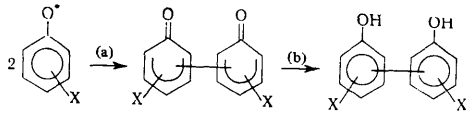
In another study [137] the rotating sector method was employed in combination with irradiation of the α-diketone in an ESR cavity in the presence of phenol. This method makes it possible to determine the rate constants for the dimerisation of phenoxy-radicals. In benzene the rate constants vary from 1.7×10^7 litre mole^{-1} s^{-1} for the *p*-methylphenoxy-radical to 4.5×10^9 litre mole^{-1} s^{-1} for the 2-naphthoxy-radical at 30°C (Table 3). As a rule, the rate constants in benzene are an order of magnitude higher than in chlorobenzene, but are smaller than k_{diff}.

Table 3. The rate constants for the destruction of phenoxy-radicals by second-order reactions.

X	Medium, temperature, °C	k/ϵ, cm s^{-1}	k, litre mole^{-1} s^{-1}	References
H	Water, 17-23	$3.5 \cdot 10^5$	$5.4 \cdot 10^8$	45
»	Water, 25	—	$5.6 \cdot 10^9$	50
»	Benzene, 29-31	—	$6.3 \cdot 10^8$	137
»	Chlorobenzene, 29-31	—	$5.5 \cdot 10^7$	137
»	Water, 12	$1.2 \cdot 10^5$	$2.8 \cdot 10^8$	72
2-CH_3[a]	Water, 12	$4.7 \cdot 10^4$	$1.6 \cdot 10^8$	72
3-CH_3	Water, 12	$2.5 \cdot 10^4$	$7.5 \cdot 10^7$	72
4-CH_3	Water, 25	$4.3 \cdot 10^5$	$6.5 \pm 0.3 \cdot 10^9$	50
»	Water, 25	$5.9 \pm 0.3 \cdot 10^5$	$1.9 \pm 0.3 \cdot 10^9$	51
»	Benzene, 29-31	—	$1.5 \cdot 10^9$	137
»	Water, 12	$4.4 \cdot 10^4$	$1.1 \cdot 10^8$	72
Tyrosine radical	Water, 25	$4.5 \pm 0.2 \cdot 10^5$	$1.2 \pm 2 \cdot 10^9$	51
»	Water, 12	$1.2 \cdot 10^5$	$2.7 \cdot 10^8$	147
4-CH_3O	Benzene, 29-31	—	$1.7 \cdot 10^7$	137
»	Chlorobenzene, 29-31	—	$1.4 \cdot 10^6$	137
2,6-Di-t-butyl-4-methyl	CCl_4, 17-23	$8.2 \cdot 10^4$	$1.5 \cdot 10^8$	45
2,6-Di-t-butyl-4-ethyl	CCl_4, 17-23	$7.4 \cdot 10^3$	$1.3 \cdot 10^7$	45
2,4-di-t-butyl	Liquid paraffin, 17-23	$1.1 \cdot 10^4$	$2.0 \cdot 10^7$	45
3-NO_2	Water, 12	$2.6 \cdot 10^4$	$1.3 \cdot 10^7$	72
2,4-Dibromo	Water, 12	$2.7 \cdot 10^4$	$1.0 \cdot 10^8$	72
4-I	Water, 20	$1.9 \cdot 10^5$	$5.5 \cdot 10^8$	146
2-OH	Water, 20	$8.0 \cdot 10^5$	$3.9 \cdot 10^8$	172
3,6-Di-t-butyl-2-hydroxy	Toluene, 27	—	$5.4 \cdot 10^8$	173

[a] E_a = 3.1 kcal mole^{-1} in toluene [11].

The activation energies for the dimerisation reactions of 14 phenoxy-radicals in benzene and chlorobenzene have been measured [176]. Comparison of these results with those obtained by the thermochemical analysis of the intermediates formed in the dimerisation reactions showed that the radicals investigated can be divided into two classes. Those for which the heat of formation of the initial intermediate (the keto-dimer) exceeds 20 kcal mole^{-1} have absolute dimerisation rate constants and activation energies which agree with the diffusion theory. For certain other radicals, for example, 4-phenyl- and 4-methoxy-phenoxy-radicals, the heat of formation of the intermediate keto-dimer is much less than 20 kcal mole^{-1} and the rate constants and activation energies differ significantly from the values predicted by the theory [176]. The final products of the destruction of PhO·, formed via the isomeric intermediate diketo-compound, are obtained as a result of the dimerisation of PhO· and subsequent enolisation with formation of the final products [137,138].



(3)

In organic solvents (benzene, chlorobenzene) stage *b* may be rate-limiting and the addition of acid sharply accelerates the process. The same mechanism of the recombination of PhO· is applicable also to an aqueous medium.

Despite the fact that the rate of process *b* should be high in an aqueous medium [176], it was found [147] that k_3 increases with decrease of pH from 8 to 1. Thus $k_3 = 1.6 \times 10^8$ litre mole^{-1} s^{-1} at pH 8 and 1.9×10^9 litre mole^{-1} s^{-1} at pH 1 for *o*-methylphenoxy-radicals. A similar conclusion can be reached by considering other experimental data [50,51].

The introduction of alkali metal salts into aqueous solutions of *o*-cresol reduces the dielectric constant of the solution and hence the rate constant for the recombination of the polar species—phenoxy-radicals [177].

The influence of atmospheric oxygen on the kinetics of the destruction of the majority of short-lived phenoxy-radicals is insignificant [72].

Disproportionation is the reaction whereby certain 4-alkyl-2,6-di-t-butylphenoxy-radicals are destroyed [13]. For example, 2,6-di-t-butyl-4-isopropylphenoxy-radicals are destroyed via second-order reactions with formation of the initial phenol and a quinone methide [48]. The deviation from second-order kinetics in the radical anihilation reaction and its occurrence in accordance with first-order kinetics, observed for 2,6-di-t-butyl-4-methylphenoxy-radicals and certain others, has been explained [45,178,179] by the isomerisation of the phenoxy-radical to the hydroxybenzyl radical with migration of the hydrogen atom of the *p*-methyl group to the phenoxy-oxygen atom. However, a more convincing explanation of the change from second-order to first-order kinetics in the radical annihilation reaction involves the formation of the intermediate 2,6-di-t-butyl-4-(2,6-di-t-butyl-4-methylphenoxy)-4-methylcyclohexa-2,6-dienone [183].

The experimental observation that there is no interconversion of the unsubstituted phenoxy- and *p*-hydroxyphenyl radicals [73] is consistent with the high activation energy for this process (more than 100 kcal mole^{-1}), calculated by the MINDO/2 method [146]. The kinetics of the reactions involving the destruction of phenoxy-radicals with comparatively complex structures have also been examined in other studies [13,180-182].

The rate of annihilation of the 2,6-di-t-butyl-4-methylphenoxy-radicals in acetonitrile in the presence of tetrabutylammonium hydroxide (TBAH) is described by a first-order kinetic equation [184]. With increase of TBAH concentration, the rate of consumption of the phenoxy-radical falls. The authors believe that TBAH forms a donor–acceptor complex with the phenoxy-radical, which may reduce the rate of consumption of the latter as a result of its stabilisation.

2. Semiquinone Radicals

The disappearance of semiquinone radicals is described by second-order kinetics. The annihilation of neutral semiquinone radicals proceeds via a disproportionation reaction:

$$QH^{\cdot} + QH^{\cdot} \rightarrow Q + QH_2, \qquad (4)$$

while the destruction of radical-anions probably involves an electron transfer reaction:

$$Q^{\cdot-} + Q^{\cdot-} \xrightarrow{+2H^+} Q + QH_2. \qquad (5)$$

The rate constants for the annihilation of neutral semiquinone radicals at room temperature in non-viscous solvents are usually about 10^9 litre mole^{-1} s^{-1} (Table 4). The diffusion constant calculated from the Debye formula is of the same order of magnitude, but, as for phenoxy-radicals, is in most cases numerically larger.

The rate constants for the destruction of radical-anions are an order of magnitude smaller than those for the destruction of the corresponding neutral radicals (Table 4). The simplest possible explanation of this finding is that, when the interaction of radical-anions is largely determined by diffusion, then the rate constant for the diffusion-controlled reaction of the charged species can be calculated from the Debye formula, which takes into account the Coulombic repulsion (or attraction):

$$k_{diff.} = \frac{8RT}{3000\,\eta} \cdot \frac{\delta}{e^{\delta} - 1},$$

where η is the viscosity of the solvent and δ a quantity which depends on the product of the charges of the reacting species. The quantity $\delta/(e^{\delta} - 1) < 1$ for species having charges of the same sign. For example, this term is 0.1 when the charges on the species are -1 and the distance of closest approach is 2 Å. [188]

Table 4. The rate constants for the destruction of semiquinone radicals via second-order reactions at about 20°C.

Initial quinone	Rate constants for annihilation reaction, mole^{-1} s^{-1}			References
	$QH^{\cdot}$	$Q^{\cdot-}$	solvent	
p-Benzoquinone[c]	$1.1 \cdot 10^9$	$1.7 \cdot 10^8$	Water	154
	$1.2 \cdot 10^9$	$5.5 \cdot 10^7$	Water[a]	163
	$1.5 \cdot 10^9$	—	Isopropyl alcohol	87
	$5.4 \cdot 10^9$	—	Dioxan	87
	$2.7 \cdot 10^8$	—	Ethanol	187
Duroquinone[d]	$1.8 \cdot 10^9$	$1.2 \cdot 10^8$	Water–propanol	185
	$7.2 \cdot 10^8$	$2.9 \cdot 10^7$	Water[a]	163
	$8.0 \cdot 10^8$	$4.6 \cdot 10^6$	Ethanol–water	89
	$7.3 \cdot 10^8$	—	Isopropyl alcohol	87
	$2.9 \cdot 10^9$	—	Dioxan	87
Chloranil	—	$4.06 \cdot 10^6$	Ethanol	88
	—	$1.16 \cdot 10^7$	Methanol	88
	$1.7 \cdot 10^8$	—	Isopropyl alcohol	87
	$8.2 \cdot 10^8$	—	Dioxan	87
1,4-Naphthoquinone	$1.3 \cdot 10^9$	$1.0 \cdot 10^8$	Water[a]	163
	$2.3 \cdot 10^8$	—	Isopropyl alcohol	87
	$9 \cdot 10^8$	—	Dioxan	87
	$2.6 \cdot 10^9$	—	Ethanol	187
Vitamin K_3	$3.4 \cdot 10^9$	$5.5 \cdot 10^8$	Water	165
	$1.3 \cdot 10^9$	$1.6 \cdot 10^8$	Water[a]	163
Anthraquinone	—	$4.9 \cdot 10^7$	Isopropyl alcohol	87
	$1.2 \cdot 10^9$	—	Dioxan	87
Anthraquinone-1-sulphonate	$1.6 \cdot 10^9$	—	Water[a]	74
Riboflavin	$1.14 \cdot 10^9$	$7.0 \cdot 10^8$	Water	105
	$3.5 \pm 0.5 \cdot 10^9$[b]	—	Water	186
	—	$(1.0 \pm 0.5) \cdot 10^8$	DMF	186
Flavin mononucleotide	$3.5 \cdot 10^8$	$1.0 \cdot 10^8$	Water	106
Lumiflavin	$(0.75-1.0) \cdot 10^9$	—	Water	113

[a] The solutions contained 1–3 M isopropyl alcohol. [b] The ionic strength was $I \simeq 0$; a decrease of the rate constant for the radical annihilation reaction has been observed [186] with increase of ionic strength. [c] For the annihilation of the neutral radical, $E_{act} = 3.7 \pm 0.3$ and 3.9 ± 0.4 kcal mole^{-1} in isopropyl alcohol and dioxan respectively [187]. [d] For the annihilation of the neutral radical, $E_{act} = 3.3 \pm 0.3$ and 3.8 ± 0.4 kcal mole^{-1} in isopropyl alcohol and dioxan respectively [87].

The kinetics of the destruction of semiquinone radicals have been studied by pulse radiolysis [115,125-129,132], flash photolysis [79,80,82,83,88,106,111,113,147,149,153] (including detection by ESR), and by ESR in combination with the rotating sector method [87,187]; some of the results are presented in Table 4.

The data in Tables 3 and 4 show that in many cases the rate constants for the annihilation of phenoxy- and semiquinone radicals differ markedly under similar conditions (data of different workers). The causes of such differences remain obscure; possibly the main errors may be attributed to an inaccurate determination of the concentration of the radicals (extinction coefficients).

It has been found[87] that the rate constants for the destruction of a number of neutral semiquinone radicals in dioxan are approximately four times greater than is isopropyl alcohol (Table 4), owing to the difference between the viscosities of these solvents. This may be an indication that the radical-annihilation reaction is diffusion-controlled[87]. Other workers[187] also believe that the rate of destruction of many neutral semiquinone radicals in organic solvents is diffusion-controlled and that rotational diffusion of the radicals in the cage is a factor which influences the rate of reaction.

The annihilation of the anthrasemiquinone radical-anion $AQ^{\cdot-}$ in isopropyl alcohol follows second-order kinetics[87]. The authors proposed the following mechanism for the destruction of $AQ^{\cdot-}$, which is apparently general for semiquinone radical-anions in organic non-alkaline media:

$$AQ^{\cdot-} + H^+ \rightleftarrows AQH^{\cdot}, \quad (6)$$

$$2\,AQH^{\cdot} \rightarrow AQ + AQH_2. \quad (7)$$

Thus the differential equation for the rate of destruction of $AQ^{\cdot-}$ is that for second-order reactions:

$$-\frac{d[AQ^{\cdot-}]}{dt} = \frac{k_7[H^+]}{k_6}[AQ^{\cdot-}]^2$$

and $k_{obs} = k_6[H^+]/k_7$.

Semiquinone radicals differ appreciably in their ability to react with oxygen, which has been the subject of a number of investigations[149,153,157,158,164,189,190]. Thus the radical-anions derived from anthraquinone-2,6-disulphonic acid ($AQ^{\cdot-}$) and the anthraquinone-2-sulphonic acid interact effectively with oxygen:

$$AQ^{\cdot-} + O_2 \rightarrow AQ + O_2^{\cdot-}$$

($k = 5 \times 10^8$ litre mole^{-1} s^{-1}, 95% of water, 5% of isopropyl alcohol–acetone mixture, 20°C [164]), while the radical-anions derived from *p*-benzoquinone ($BQ^{\cdot-}$) do not interact[149,164]. The reverse process—the transfer of an electron from the superoxide ion to the quinone—has been studied for *p*-benzoquinone and a number of other quinones (trimethylbenzoquinone, vitamin K_3, etc.)[157,189,190]:

$$BQ + O_2^{\cdot-} \rightarrow BQ^{\cdot-} + O_2$$

($k = 9.6 \times 10^8$ litre mole^{-1} s^{-1}, aqueous solution containing 1 M t-butyl alcohol, 20°C [157]). Duroquinone (DQ) is involved in the reversible reaction

$$O_2^{\cdot-} + DQ \rightleftarrows O_2 + DQ^{\cdot-} \quad (8)$$

[$K_{C_8} = (2.3 \pm 0.2) \times 10^{-2}$, 95% of water, 5% of isopropyl alcohol–acetone mixture, 20°C].[164] The semiquinone radicals formed in the photochemical reduction of quinones do not react with the solvent radicals (radical-cations)[88]. However, the semiquinone radicals obtained as a result of the photochemical oxidation of inorganic anions by excited quinone molecules or in the photochemical reduction of quinones by excited pigment molecules interact effectively with the radical-anions and radical-cations formed[141,152,153]. For example, the radical-anion derived from anthraquinone-2,6-disulphonic acid ($AQ^{\cdot-}$) is destroyed via the reactions

$$AQ^{\cdot-} + CO_3^{\cdot-} \rightarrow AQ + CO_3^{2-}, \quad (9)$$

$$AQ^{\cdot-} + Chl^{\ddagger} \rightarrow AQ + Chl, \quad (10)$$

where $k_9 = 1.4 \times 10^9$ litre mole^{-1} s^{-1} in aqueous solution and $k_{10} = 2.3 \times 10^9$ litre mole^{-1} s^{-1} in methanol at room temperature, $Chl^{\ddagger}$ being the chlorophyll radical-cation[152].

VIII. INTERACTION WITH METAL COMPOUNDS

The study of the mechanisms of the inhibiting and catalytic effects of metal compounds in liquid-phase oxidation reactions is closely associated with the study of the joint action of these compounds with a series of important inhibitors (phenols, hydroquinone, catechol, and others). The corresponding phenoxy- and semiquinone radicals formed in the system can interact with the metal compounds. In many chemical and biochemical systems, where phenoxy- and semiquinone radicals are formed, transition metal ions and compounds are present and therefore the study of the interaction of these radicals with metal compounds is of considerable interest. Radical reactions of this type have been comparatively little investigated, although they are of fundamental importance both for the chemistry of free radicals and for the elucidation of the mechanisms of many processes in homogeneous catalysis.

It has been shwon[147] that the interaction of phenoxy- and semiquinone radicals with transition metal compounds proceeds via one of the following pathways.

$$R^{\cdot} + M^{n+}Li_m \begin{cases} \rightarrow R^{\pm} + M^{(n\mp1)+}Li_m & \text{electron transfer,} \quad (11) \\ \rightarrow RML_{m-1} + Li & \text{ligand substitution,} \quad (12) \\ \rightarrow R^{\cdot} \ldots M^{n+}Li_m & \text{formation of charge-transfer complex.} \quad (13) \end{cases}$$

If reactions (11)–(13) are not dominant, then reactions (3)–(5) as a rule occur simultaneously in the system.

A change in the absorption spectrum and in the kinetics of the destruction of *o*-methylphenoxy-radicals has been observed[177] in an acid aqueous solution containing CuCl, owing to the formation of a charge-transfer complex. Spectroscopic-kinetic evidence for the existence of complexes of *o*-methylphenoxy-radicals with Cu^{2+}, Mn^{2+}, and Fe^{2+} ions was obtained similarly. The bond in the complexes is fairly weak and their formation in a polar medium is a reversible process, since their dissociation is facilitated by solvation of the ion and radical formed. The stabilisation of phenoxy-radicals due to the formation of their complexes can be observed in media of low polarity[11].

Pulse photoexcitation of *o*-cresol in benzene, toluene, and hexane leads to the formation of the *o*-methylphenoxy-radical ($\lambda max = 405$ nm in all solvents)[11]. The introduction of cobalt acetylacetonate as an additive into the solutions alters the absorption spectra of the intermediates by causing the appearance of a new absorption band in the range 440–450 nm. Such changes in the absorption spectra of the *o*-methylphenoxy-radical are due to the formation of a complex by the fast reaction

$$PhO^{\cdot} + Co(acac)_2 \rightarrow PhO^{\cdot} \ldots Co(acac)_2. \quad (14)$$

The destruction of phenoxy-radicals and their complexes with $Co(acac)_2$ follows second-order kinetics:

$$2PhO^{\cdot} \ldots Co(acac)_2 \rightarrow \text{products.} \quad (15)$$

It was observed that $k_{15} < k_{14}$. The activation energies for the annihilation reactions of the phenoxy-radicals and their complexes in benzene were found to be 3.1 and 6.5 kcal mole^{-1} respectively. The decrease in the rate constant for the destruction of the complexes and the increase in the activation energy compared with the destruction of

the phenoxy-radicals themselves shows that $Co(acac)_2$ behaves kinetically as a spatially bulky substituent in the phenoxy-radical[11]. Changes in the absorption spectrum and in the kinetics of the destruction of the *p*-methylphenoxy-radical, indicating the formation of a new species (complex), were observed in the flash photolysis of *p*-cresol in toluene in the presence of $Fe(acac)_2$.[147]

Aromatic compounds are known to be capable of forming complexes with transition metal ions and coordination compounds. This applies particularly to aromatic free radicals. The difference is that, in the formation of a complex by an unstable (in the thermodynamic sense) radical and the metal compound, the free valence is not as a rule annihilated and complexes of this type are also unstable. The unpaired electron is then delocalised over the electron shell of the metal, which may increase the relative stability of the complex.

The existence of a complex of the stable 2,4,6-tri-t-butylphenoxy-radical and $Co(acac)_2$ has been observed by ESR.[191] An interaction was discovered between the unpaired electron and the cobalt nucleus; in addition to a triplet corresponding to the phenoxy-radical, an octet due to the presence of the complex was found.

It has been concluded[11] that $Co(acac)_2$ must nave the properties of an inhibitor of liquid-phase chain oxidation reactions of hydrocarbons. Indeed, the study of the liquid-phase oxidation of cumene and the presence of $Co(acac)_2$ showed that the latter behaves as a powerful inhibitor. The oxidation of cumene in the presence of *o*-cresol and $Co(acac)_2$ is a complex process in which the intermediate complex of the *o*-methylphenoxy-radical with a chelate plays a definite role and influences the induction period[192].

The absorption spectrum of the *p*-benzoquinone radical-anion ($Q^{\cdot-}$) has been recorded in a water–propanol solvent during the flash photolysis of hydroquinone (QH_2).[193] The disappearance of the $Q^{\cdot-}$ absorption bands and the appearance of bands due to other intermediates formed via the reactions

$$Q^{\cdot-} + Cu^{+} \rightleftarrows X_1^{\cdot} \qquad (16)$$

$$Q^{\cdot-} + Cu^{2+} \rightleftarrows X_2^{+} \qquad (17)$$

was observed in the photolysis of QH_2 in the presence of Cu^{+} and Cu^{2+}. The complexes were shown to have the 1 : 1 compositions. The equilibrium constants for reactions (16) and (17) were calculated with the aid of the relation

$$\frac{1}{[X_{1,2}^{\cdot}]} = \frac{1}{K_i[Q^{\cdot-}]_0 \cdot [Cu^{n+}]} + \frac{1}{[Q^{\cdot-}]_0}.$$

The two reactions are between ions bearing charges of different sign and therefore, other conditions being equal, K_{17} should be larger than K_{16}, which is consistent with the experimental values obtained: $K_{16} = 7.0 \times 10^3$ litre mole^{-1} and $K_{17} = 1.0 \times 10^4$ litre mole^{-1} at 20°C. The importance of the Coulombic interaction in the formation of these complexes is noteworthy. When QH_2 was introduced into an acid solution (at pH 1.0; the radical $QH^{\cdot}$ is then formed), of the salts CuCl and $CuSO_4$, the formation of complexes with $QH^{\cdot}$ was not observed; the absorption spectra of the intermediates were the same as those of $QH^{\cdot}$ and the effect on the kinetics of the annihilation of $QH^{\cdot}$ was insignificant. Calculations by the MINDO/2 method of the charges on the oxygen atoms in the water molecule, the neutral *p*-benzosemiquinone radical, and the corresponding radical-anion showed that the highest charge is that of the oxygen atom in the radical-anion, which displaces a water molecule from the coordination sphere of the copper ion, and the smallest charge is in the neutral benzosemiquinone radical, which did not form any complexes. Thus the complex-formation reaction is apparently a nucleophilic substitution process[147].

The kinetics of the destruction of radical species in the systems investigated were second-order[193]:

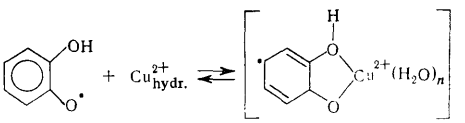
$$X_1^{\cdot} + X_1^{\cdot} \rightarrow \text{products.} \qquad (18)$$

$$X_2^{+} + X_2^{+} \rightarrow \text{products.} \qquad (19)$$

In a water–propanol medium at 20°C, $k_{18} = 1.6 \times 10^7$ and $k_{19} = 3.8 \times 10^6$ litre mole^{-1} s^{-1} at an ionic strength $I = 0$.

The above values of k_{18} and k_{19} show that the interaction of the semiquinone radical with copper ions lead to the formation of more stable radical species. The increased stability of the complexes compared with the initial radical can be caused by the partial delocalisation of the unpaired electron over the electron shell of copper and possibly by the appearance of steric hindrance in the recombination of the complexes. *o*-Benzosemiquinone and flavosemiquinone radicals can give rise to radical complexes, behaving as bidentate ligands. *o*-Benzosemiquinone radical-anions and their derivatives form complexes with many Group I–III metal ions and certain others[194–197]. These complexes, which have been investigated by ESR, consist of contact or solvent-separated ion pairs[197] or inner-sphere complexes[172,194].

The absorption spectrum of the neutral *o*-benzosemiquinone radical, obtained in a water–propanol solution in the flash photolysis of catechol has been recorded[172]. The *o*-benzosemiquinone radical forms an inner-sphere complex with the Cu^{2+} ion, where apparently $n \leq 4$:



The spectroscopic-kinetic characteristics of this complex, the complex formation constants and the rate constant for its formation and decomposition, have also been obtained. It has been established that the complex has the 1 : 1 composition. The rate constant for the destruction of the complex is two orders of magnitude larger than the rate constant for the disproportionation of *o*-benzosemiquinone radicals ($I = 0$). Thus the formation of the complex stabilises the radical as a result of the screening of the reaction centre by the oxygen atom and the delocalisation of the unpaired electron over the electron shell of the Cu^{2+} ion[172].

The study of the interaction of various flavin radical compounds with metal ions is important in the investigation of the nature of the active centres in metal-containing flavoproteins.

The complexes of flavosemiquinone radical-anions and Zn^{2+} and Cd^{2+} ions have been investigated[127,170,198,199] by electronic spectroscopy and ESR. The equilibrium

$$Fl + FlH_2 \rightleftarrows 2FeH^{\cdot}$$

shifts to the right in the presence of these metal ions:

$$Fl + FlH_2 + 2M^{2+} \rightleftarrows 2[FlM]^{+} + 2H^{+}.$$

The spin concentration then increases by a factor of 15, reaching approximately 34% of the total concentration of the flavin. It was shown that certain neutral flavosemiquinone radicals, with electron-donating substituents in the isoalloxazine ring, are capable of forming complexes with these ions[127].

The absorption spectrum of the $Fl^{\cdot-}$ radical-anion was recorded in the photoexcitation of riboflavin in dimethylformamide in the presence of a base[186]. The destruction of $Fl^{\cdot-}$ follows second-order kinetics:

$$Fl^{\cdot-} + Fl^{\cdot-} \rightarrow \text{products.} \quad (20)$$

In the presence of the salts $CdCl_2$ and $ZnSO_4$ the kinetics of the destruction of the intermediate compounds consist of two components (fast and slow). Reactions (20) and (21) correspond to the fast component:

$$Fl^{\cdot-} + M^{2+} \rightarrow \dot{F}l\,M^{+}, \quad (21)$$

and the annihilation of the complexes formed corresponds to the slow component:

$$\dot{F}lM + \dot{F}lM^{+} \rightarrow \text{products.} \quad (22)$$

$k_{22} = 2.5 \times 10^6$ and 1.0×10^6 litre mole^{-1} s^{-1} for the cadmium and zinc complexes respectively[186]. The flavosemiquinone radical-anion behaves as a bidentate ligand capable of forming complexes with metal ions having *d* electrons. On formation of the complex, the unpaired electron is delocalised over the electron shell of the metal, which stabilises the radical. The formation of a complex by the radical and the metal ion leads to a change in the redox potential. In relation to biological oxidation-reduction processes involving organometallic flavoenzymes, this implies that the system can embrace a wide range of potentials, undergoing not only $Fl \rightleftarrows FlH_2$ but also $Fl \rightleftarrows MFl^{\ddagger}$ and $MFl^{\ddagger} \rightleftarrows FlH_2$ transitions[127,186].

The complexes formed by paramagnetic ligands with diamagnetic metal ions are very rare. They are of interest for the investigation of the nature of the metal–ligand bond and also for the formation of spin labels bound to the metal in enzymes. The use of such labels is extremely promising in the study of the properties of enzymes, since it must involve the transfer of spin via the metal to the remaining parts of the ligand environment.

The absorption spectrum of the flavosemiquinone radical $FlH^{\cdot}$ has been recorded in the flash photolysis of riboflavin in water. The introduction of metal salts (including those of cadmium and zinc) into an aqueous flavin solution did not result in the formation of complexes. Some decrease of k_{20}, caused by the increase of the ionic strength, was then observed. Thus the *p*-benzosemiquinone radical can serve as a model for the elucidation of complex-formation processes involving more complicated semiquinone radicals: the $Fl^{\cdot-}$ radical-anion can form complexes with metal ions, in contrast to the neutral radical $FlH^{\cdot}$.[147]

Apart from the complex-formation reactions with transition metal ions, oxidation-reduction reactions have been observed for semiquinone radicals.

The influence of Cu^{+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Mn^{2+}, Ho^{3+}, Cd^{2+}, Co^{2+}, Mg^{2+}, Hg^{2+}, Zn^{2+}, Ni^{2+}, and K^{+} ions on the kinetics of the annihilation of the radical-anions obtained from 2-methyleneanthraquinone has been studied[149]. In certain cases the metal ions greatly reduced the lifetime of the radicals, although in others they had little or no influence on the kinetics of the destruction of the radical-anion. On average, paramagnetic ions had a greater effect than diamagnetic ions. The sharp decrease of the lifetime of the radical, observed when Cu^{2+} and Fe^{3+} ions are added, is due to the oxidation of the semiquinone by the metal ion:

$$M^{n+} + SQ^{\cdot-} \rightarrow M^{(n-1)+} + SQ.$$

p-Benzoquinone radicals are involved in oxidation-reduction reactions with iron ions. The reactions

$$Q^{\cdot-} + Fe^{2+} \xrightarrow{+2H^{+}} QH_2 + Fe^{3+}, \quad (23)$$

$$QH^{\cdot} + Fe^{2+} \xrightarrow{+H^{+}} QH_2 + Fe^{3+}, \quad (24)$$

$$QH^{\cdot} + Fe^{3+} \xrightarrow{-H^{+}} Q + Fe^{2+} \quad (25)$$

in aqueous propanol have been investigated by flash photolysis[185]. The rate constants $k_{23} = 4.3 \times 10^5$, $k_{24} = 1.5 \times 10^5$, and $k_{25} = 7.0 \times 10^5$ litre mole^{-1} s^{-1} were obtained at 20°C. It is suggested that the oxidation-reduction reactions between transition metal ions and organic radicals proceed via the formation of a complex of the radical with the metal ion, which decomposes with formation of the reduction products of the radical and oxidation of the ion[200]. Possibly reactions (23) and (24) proceed via the same mechanism and the observed rate constants refer to the rate-limiting stage of this two-stage process[185].

IX. SOME QUANTUM-CHEMICAL CALCULATIONS ON PHENOXY- AND SEMIQUINONE RADICALS

Phenoxy- and semiquinone radicals have been the subject of a number of theoretical investigations[20,201–205]. Attention was concentrated on the calculation of the distribution of spin densities. Calculations on phenoxy-radicals by the Hückel molecular orbital method lead to a poor agreement with experiment[201]. In calculations of spin densities, Porter and coworkers[202] took into account the contributions of five excited doublet states, which led to a qualitative agreement with ESR data.

Calculations of spin density in a number of phenoxy-radicals by the molecular orbital method in terms of the Hückel and McLachlan approximations and by the valence bond method led to results in agreement with experiment[203]. The distribution of spin density in benzosemiquinone radical-anions has been calculated[204] by the LCAO-SCF-MO method in terms of the McLachlan approximation with variation of the molecular orbital parameters; the results of the calculation are in good agreement with experiment.

INDO calculations have been made on the simplest phenoxy-radical[20]. The geometry of the phenoxy-radical, the π-electronic charges on its O and C atoms, the hyperfine coupling constants, and certain other parameters were evaluated. It was found that, compared with the isoelectronic benzyl and anilino-radicals, the benzene ring is least distorted in the phenoxy-radical. A similar conclusion may be reached by considering the contributions of various valence bond schemes to the radical structure. An *ab initio* calculation has been made[205] for the unsubstituted phenoxy-radical. The electronic, nuclear, and total energies of the radical, the eigenvalues of a series of operators for various wave functions, and the hyperfine coupling constants were obtained; these data are in qualitative agreement with experimental results. In general *ab initio* calculations on such systems give a less satisfactory agreement with experimental data than calculations by semiempirical methods.

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The Electronic Structure and Reactivity of Cyclohexadienone Carbenes

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The structure, multiplicity of the electronic states, and reactivity of cyclohexadienone carbenes are discussed. The literature on the chemical behaviour of such carbenes has not previously been surveyed. Only monocylic carbenes of the above type are considered.
The bibliography includes 70 references.

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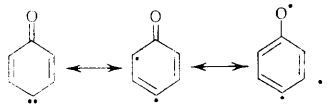
I. INTRODUCTION

Derivatives of bivalent carbon (carbenes) have continually attracted the attention of chemists in various countries. This is because of the possibility of calculating relatively easily by quantum-mechanical methods the structures of the simplest carbenes and of investigating the reactivities of these species as a function of their structure. Furthermore, a wide variety of carbenes are used extensively in preparative organic chemistry. For this reason, a series of monographs and reviews have been devoted to the chemistry of carbenes [1-9]. The chemical behaviour of cyclohexadienone carbenes differs very sharply from that of carbenes of other types. Various aspects of their structure and chemical reactions are important for theoretical organic chemistry, but have not previously been discussed in the literature.

Monocyclic carbenes of this type are used successfully in the synthesis of derivatives of sterically hindered phenols, which are inhibitors of radical processes [10]. Vigorous research is being prosecuted at the Institute of Chemical Physics of the USSR Academy of Sciences under the supervision of Academician N. M. Emanuel' on the applications of typical radical process inhibitors in various fields of experimental medicine, biology, and chemistry [11]. Sterically hindered phenols and their derivatives are employed most widely as inhibitors of the thermo-oxidative degradation of polymeric materials, oils and fuels.

II. ELECTRONIC STRUCTURE OF CYCLOHEXADIENONE CARBENES

The cyclohexadienone carbenes are a special type of cyclic carbenes whose conjugated system exhibits a very marked tendency towards the formation of an aromatic structure. Following the abstraction of the nitrogen molecule from the initial diazo-oxide†, the non-bonding electrons in the resulting cyclohexadienone carbene may be initially distributed between the σ and p_z orbitals. As in the case of cyclopentadienylidene, the electron in the p_z orbital can interact with the π-electron system of the diene. In cyclopentadienylidene this interaction leads only to the stabilisation of the triplet form without any rearrangement of the overall electronic structure of the molecule. On the other hand, in cyclohexadienone carbenes an aromatic structure is formed with an energy gain owing to conjugation (approximately 1.5 eV). The redistribution of electrons results in the formation of the carbene, which can be characterised by the following set of structures:



The distribution of non-bonding electrons is such that the σ-electron system of cyclohexadienone carbenes is to a large extent similar to that of the phenyl radical and their π-electron system is similar to that of phenoxy-radicals.

The general characteristics of the electronic structure of cyclohexadienone carbenes lead to the conclusion that their lifetime in the ground state (at any rate at low temperatures in an inert matrix) should be much longer than that of the simplest methylenes. This is confirmed by ESR data [12,13]. The ESR spectrum of unsubstituted cyclohexadienone carbene, obtained in the photolysis of benzene 1,4-diazo-oxide using filtered light in a *p*-dichlorobenzene matrix at the temperature of liquid nitrogen, consists of several signals. The most intense signal is located at zero field, while the remaining signals, with decreasing intensities, are in the region of 4550, 4770, and 6670 G. The observed signals have a very remarkable fine structure—they all exhibit distinct multiplet splitting. The observed splittings correspond to the spin–spin interaction of the unpaired p_z electron with the *ortho*- and *meta*-protons in the ring. Following the substitution of both *ortho*-positions of the carbenes by t-butyl groups or chlorine atoms, the signals become triplets.

At low temperature in an inert matrix, the signals of triplet carbene are observed virtually unchanged for a long time (1–1.5 h) in the absence of additional irradiation. This shows that the cyclohexadienone carbenes have a triplet ground state.

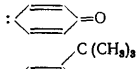
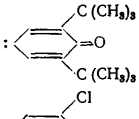
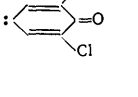
The reactivity of cyclic carbenes is determined by nucleophilic or electrophilic properties. Since the number of π electrons in the ring determines the net spin of the ground state of cyclic carbenes [14], appreciable differences are to be expected in their behaviour depending on the number of these electrons. In carbenes with the $(4n + 2)$

†The possibility of the generation of cyclohexadienone carbenes by the photolysis and thermolysis of arene diazo-oxides has been considered [11-13].

π-electron system the σ^2 configuration is stabilised and they have a singlet ground state with a vacant p_z orbital at the carbene centre. The vacant p_z orbital is incorporated in the overall π-electron system of the carbene molecule, which leads to the appearance of an enhanced electron density at the central carbon atom. Such carbenes are nucleophilic in the ground state. On the other hand, in carbenes with the $(4n)$ π-electron system the σ_p configuration is stabilised and they have a triplet ground state; such carbenes exhibit electrophilic properties.

In cyclohexadienone carbenes the incorporation of the p_z orbital of the central carbon atom in the overall π-electron system of the polyene part of the molecule leads to a shift of the p_z electron and the formation of an aromatic ring system. As a result, the electron density at the central carbon atom should fall. Their chemical behaviour resembles that of carbenes with the $(4n)$ π-electron ring system, i.e. they should be electrophilic. This conclusion is confirmed by ESR data [12,15-17]. The Table lists the splitting parameters of the energy levels of triplet methylenes at zero field. The D parameter characterises the spin–spin interaction of the unpaired electrons and is determined by the average value of the quantity $(1/r^3)$, [18,19] where r is the distance between the spins. This parameter may serve as a measure of the delocalisation of the p_z electron over the system of conjugated bonds and may characterise the electrophilic properties of the carbene centre. The Table shows that D is a minimum for cyclohexadienone carbene.

The splitting parameters of the energy levels of triplet methylenes at zero field.

Carbene	D, cm^{-1}	E, cm^{-1}	Valence angle, deg	References
$:CH_2$	0.6881	0.00346	136	15
$:CHC_6H_5$	0.5150	0.02510	140—155	16
$:C(C_6H_5)_2$	0.4055	0.01940	140—155	16
	0.4089	0.01200	—	17
	0.3179	0.00550	—	12
	0.3141	0.00510	—	12
	0.3284	0.00860	—	12

Since, according to its physical interpretation, the parameter D defines the probability of localising the unbound p_z electron at the bivalent carbon atom of the carbene, it follows (assuming identical distributions of π electrons in carbenes and the corresponding radicals) that the values of D for carbenes and the spin densities ρ_i for the radicals (at the same carbon atom) should be approximately the same [12,16]. Accordingly, as stated above, the π-electron system of cyclohexadienone carbenes is close to that of the corresponding phenoxy-radicals.

The parameter E characterises qualitatively the deviation of the spin–spin interaction from cylindrical symmetry and is therefore a criterion of the curvature of the methylene structure [20,21]. The E/D ratio corresponds to the contribution of the s orbital to the non-bonding sp^2 orbital of the bivalent carbon atom. For $E = 0$ $(E/D = 0)$, the contribution of the s orbital is zero, i.e. the non-bonding hybridised sp^2 orbital, located in the plane of the methylene molecule, is transformed into a pure p orbital and the methylene structure becomes linear (valence angle $\varphi = 180°$). Judging from the values of E quoted, in cyclohexadienone carbenes this angle should approach 180°. However, there is no reason to suppose that the valence angle differs appreciably from 120°. Presumably the σ bonds in the ring at the carbene centre are bent (a type of "banana bond"). In this structure for cyclohexadienone carbenes, ring strain is eliminated on the one hand and on the other there appears the possibility of a redistribution of the non-bonding σ electron among the neighbouring carbon atoms, which stabilises the carbene system as a whole.

III. THE MULTIPLICITY OF THE ELECTRONIC STATES OF REACTING CYCLOHEXADIENONE CARBENES

It was shown above that cyclohexadienone carbenes have a triplet ground state. However, the multiplicity of the ground state of the carbene frequently does not coincide with the multiplicity of its state when undergoing reaction. For synthetic use, it is essential to know the multiplicity of the electronic state of the carbene at the instant of its interaction with the substrate.

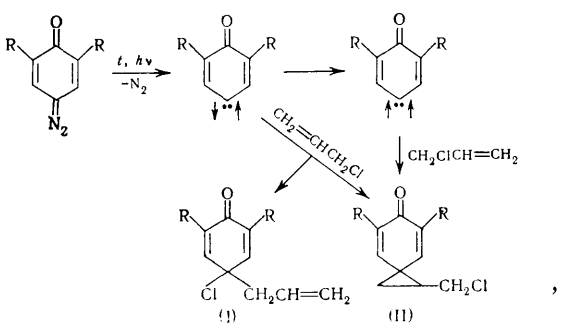
Chemical methods are nowadays widely used to determine the spin state of reacting carbenes. Thus the stereospecificity of the addition reactions of carbenes is due to the differences between the mechanisms of the interaction of the singlet and triplet forms of the carbene with the multiple bonds of *cis*- and *trans*-olefins (Skell's principle [22]). According to the majority of investigators, singlet carbenes add synchronously to the multiple bond without affecting the configuration of the initial olefin, while the triplet form reacts with formation of a trimethylene biradical, which leads to the formation of a mixture of the *cis*- and *trans*-adducts owing to the possibility of rotation about the C–C bond in the biradical (breakdown of stereospecificity). Studies on the interaction of cyclohexadienone carbenes with the multiple bonds in *cis*- and *trans*-olefins indicate a high stereospecificity of the addition (to an extent greater than 98%) in both thermal [24] and photolytic [23] formation of cyclohexadienone carbenes. This shows that the singlet form of the cyclohexadienone carbene is involved in the reaction.

Since cyclohexadienone carbenes have a triplet ground state, it follows, by analogy with gas-phase reactions, that, following the addition of an inert polyfluorinated solvent to the reacting substrate, the stereospecificity of the addition presumably breaks down in consequence of the $S \rightarrow T$ transition of the carbene when it collides with the molecules of the diluent. However, this effect (in a highly attenuated form only) was observed in the photolysis of arene diazo-oxides by filtered light at 0°C [23] and was completely absent in the thermolysis of arene diazo-oxides at 93–96°C. [24] The explanation is that at elevated temperatures the temperature conditions in the reaction, and not the effect of dilution by the polyfluorinated solvent, play a more significant role in the competition between two processes: the addition of singlet carbene to the multiple bond and the $S \rightarrow T$ transition.

The stereochemical method for the determining of the multiplicity of the electronic states of carbenes is in many cases ineffective, since, depending on the relative rates

of the intermediate stages, identical substances may be formed from both singlet and triplet carbenes [8]. For this reason, studies are now being made to discover rigorously specific reactions, which would proceed only with the triplet or singlet forms of carbenes. Research on competing reactions involving the addition of carbenes to multiple bonds and lone electron pairs of heteroatoms is extremely promising in this connection. Singlet carbenes can add both to a double bond and to lone electron pairs of a heteroatom. On the other hand, for triplet carbenes, as for other radical species, the mode of attack depends on the bond energies in the substance. Thus, in the reaction of triplet carbenes with olefins containing a halogen in the hydrocarbon chain, the double bond is most susceptible to radical attack. Consequently, the multiplicity of the electronic states of the reacting carbenes and the possibility of the $S \rightarrow T$ transition can be inferred from the change in the ratio of the yield of products resulting from the insertion of the carbene in carbon–halogen bonds to the yield of products formed as a result of the addition of the carbene to multiple bonds. This ratio decreases with increase of the fraction of the triplet form of the carbene and increases with increase of the fraction of the singlet form [25,26].

In order to investigate the multiplicity of the states of cyclohexadienone carbenes, a somewhat modified method of competition kinetics was employed [24]. The authors used allyl chloride as the substrate and, in order to increase the probability of the $S \rightarrow T$ transition, the temperature was reduced and allyl chloride was diluted with an inert solvent (hexafluorobenzene). The use of allyl chloride in the thermolysis and photolysis of 2,6-di-t-butylbenzene 1,4-diazo-oxide enabled the authors to obtain reaction mixtures consisting of a few final products suitable for spectroscopic analysis:

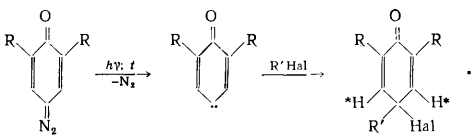


where R = $C(CH_3)_3$.

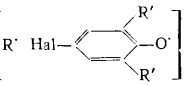
Analysis of ultraviolet spectroscopic and ^1H NMR data showed that the yields of the cyclohexadienone (I) and the spirodienone (II) and their ratio remain constant up to temperatures close to the glass point of allyl chloride. This shows that in the above temperature range the rate of reaction of the singlet carbene with allyl chloride greatly exceeds the rate of its singlet–triplet transition. With the formation of the allyl chloride matrix, the yield of I falls and that of II rises, which indicates an increasing role of the $S \rightarrow T$ transition. Evidently, on formation of the allyl chloride glass, the process becomes heterogeneous and takes place at the interface between the solid phases. The rate of reaction of the singlet carbene is now determined by its diffusion to the walls of the "cage" and may be close to the rate of the $S \rightarrow T$ transition. A further decrease of temperature tends to increase the difference between the rates of the chemical and physical processes. In contrast to the method involving a decrease of temperature, the use of the dilution technique leads to a very slight increase in the fraction of the triplet carbene. This agrees with data obtained in a study of the stereospecificity of the addition of cyclohexadienone carbenes to olefins.

In concluding this section, the possibility of employing the method of chemically induced dynamic nuclear polarisation (CIDNP) in the investigation of the multiplicity of the states of reacting carbenes must be considered. The polarisation of nuclei in the reactions of carbenes was observed for the first time by Closs and Closs [27]. Using the reactions of diphenylcarbene, they clearly formulated for the first time the idea of the selection of radicals in terms of their nuclear-spin states in the singlet–triplet transitions in radical pairs, which became the basis of the theory of the CIDNP method [28]. The method was used to investigate the thermolysis and photolysis of arene diazo-oxides [29-31].

The principal products of the thermolysis and photolysis of arene diazo-oxides in carbon tetrachloride and hexachloroacetone are the corresponding cyclohexadienone derivatives:



Their formation may be both a consequence of the rearrangement of the ylids arising in the interaction of the singlet carbene with the lone electron pairs of the halogen atom and of a radical process of the "abstraction-recombination" type. In the latter case both the singlet and triplet forms of the carbene may be responsible for the development of the reaction. Analysis of the ^1H NMR spectra of the reaction mixtures revealed a negative polarisation of the ring protons. This shows that the thermolysis and photolysis of arene diazo-oxides proceed via a radical mechanism with formation of the radical pair



as an intermediate, for which $g_{PhO\cdot} < g_{R\cdot}$ and $a_{meta} < 0$. According to the theory of CIDNP, the negative polarisation of the *meta*-protons in the recombination product of the radical pair arises when the pair was in a triplet state or when the pair was formed from the combination of independent radicals (a pair with non-correlated spins).

It was shown above that, under the usual conditions in the reaction with olefins, the carbenes are in the singlet state. Presumably cyclohexadienone carbenes also react in the singlet form with halogeno-derivatives. A singlet radical pair must then be formed initially. The radicals of this pair can recombine with the formation of cyclohexadienones or they can pass into the bulk phase, thereby producing pairs with non-correlated spins. In the former case positive polarisation of the *meta*-protons should be observed and in the latter negative polarisation. An overall polarisation has probably been observed [29-31], with the polarisation generated in the pairs with non-correlated spins predominating. This has been confirmed by experiments where radical acceptors (alkyl iodides) were added to the reaction medium [29,30]. The authors showed that, with increase of the concentration of alkyl iodides in the initial reaction mixture, the negative polarisation diminishes; at fairly high concentrations of alkyl iodides the sign of the polarisation is reversed. Evidently, following the

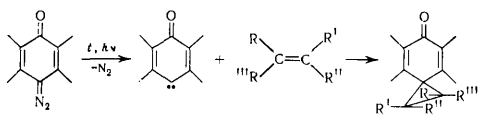
addition of alkyl iodides to the main solvent, the steady-state concentration of the radicals released into the bulk phase (particularly the $\cdot CCl_3$ and $\cdot CCl_2COCCl_3$ radicals) decreases and the contribution to the polarisation of the recombination of secondary radical pairs with non-correlated spins falls. The absorption by the *meta*-protons of cyclohexadienone compounds observed in the ^1H NMR spectra at high concentrations of alkyl iodides in the initial mixture arises because they are formed only from the primary singlet radical pairs. The polarisation of the ^{13}C nuclei[29,30] also confirms the primary formation of singlet radical pairs in the reactions of similar carbenes with hexachloroacetone.

Thus ESR and NMR data, the results of studies on the multiplicity of the states of cyclohexadienone carbenes by the method of competitive kinetics, and the high stereospecificity of their addition to the multiple bonds of olefins show that the carbenes have a triplet ground state and that under the usual conditions their reacting form is in the singlet state.

IV. REACTIONS OF CYCLOHEXADIENONE CARBENES

Addition to Multiple Bonds

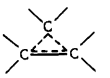
The interaction of cyclohexadienone carbenes with olefins has been most widely investigated[23,24,32-35]. The reaction with the multiple bonds of olefins of the cyclohexadienone carbenes produced by the thermolysis or photolysis of benzene 1,4-diazo-oxides results in the formation of the corresponding spirodienones containing the cyclopropane ring:



The maximum yields of the spiro-derivatives are obtained when olefins with a more nucleophilic double bond are used[32]. The introduction of functional groups into the olefin appreciably reduces the yield of the spirodienone, which is evidently associated with the ease of polymerisation of such olefins and with the difficulty of isolating the final products.

As mentioned above, cyclohexadienone carbenes add to stereoisomeric olefins with a high degree of stereospecificity[23,24,33]. Polarisation could not be observed in a CIDNP study of the thermolysis of 2,6-di-t-butylbenzene 1,4-diazo-oxide in hept-1-ene and cyclohexene [24], which confirms the conclusion that singlet carbene is involved in the reaction.

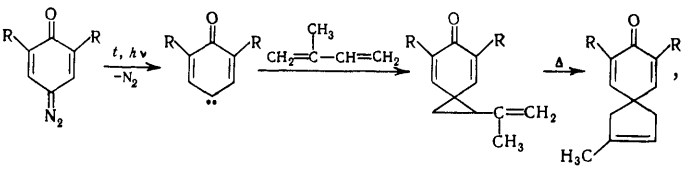
The single-stage addition characteristic of singlet carbenes is in reality more complex. The operation of dispersion forces, i.e. the interaction of the dipole moment of the carbene with the induced dipole of the olefin, leads to asymmetric addition. The non-synchronous formation of the two cyclopropane bonds is a characteristic feature of this process. Calculation shows[36] that, in the interaction of singlet methylene with ethylene, symmetrical addition is forbidden and the reaction pathway is asymmetric—it begins via an approximately π-electron mechanism and ends via an approximately σ-electron mechanism. The formation of a transition state with some sharing of the charge between the bivalent carbon of the carbene and the π bond of the olefin is then postulated:



The existence of a transition state having such a structure has been confirmed by kinetic data for dichloro- and difluoro-methylenes[37,38].

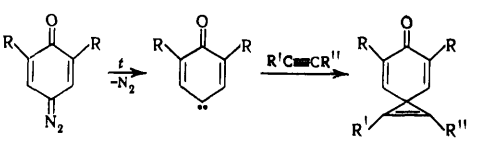
An alternative mechanism for the formation of spirodienones may involve the intermediate formation of unstable spiropyrazolones when the initial arene diazo-oxide adds to the double bond of olefins. Such adducts have been isolated in the thermolysis of 10-diazoanthrone in olefins[34]. However, this pathway is probably secondary and hardly occurs in the thermolysis and photolysis of benzene 1,4-diazo-oxides.

In the interaction of cyclohexadienone carbenes with the conjugated system of dienes, 1,2-addition to the most open double bonds might have been expected by analogy with other carbenes. However, cyclohexadiene carbenes behave in an unusual manner in this reaction—the final result is always the 1,4-addition product regardless of the presence and positions of substituents in the diene[39]. The formation of these products can be represented, on the one hand, as a result of direct 1,4-addition of the carbene to the conjugated bonds of the diene and, on the other hand, as a result of the isomerisation during the course of the reaction of the initially formed 1,2-addition product. A kinetic and spectroscopic study of the photolysis of 2,6-di-t-butylbenzene 1,4-diazo-oxide showed that in isoprene at low temperatures the second pathway is followed[39]. The authors succeeded in detecting spectroscopically and then in isolating the intermediate 1,2-addition product. Comparison of the kinetics of the isomerisation of this product and of the thermolysis of the 1,4-diazo-oxide in isoprene confirmed the proposed mechanism of the formation of the 1,4-addition product:



where $R = C(CH_3)_3$.

In contrast to double bonds, triple bonds do not exhibit a marked capacity for combination with electrophilic carbenes[40,41]. The yield of the corresponding cyclopropene derivatives in such reactions is as a rule low[40]. The reaction of cyclohexadienone carbenes with acetylenes leads to the formation of spiro[2,5]octa-1,3,6-triene-5-ones—cyclopropene derivatives of a new type in which the cyclopropene and cyclohexadienone rings are linked in a spiro-configuration[42-45]:

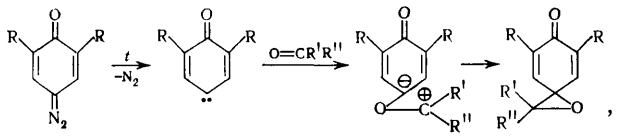


where $R = C(CH_3)_3$.

The yield of these derivatives does not exceed 40% and side products resulting from the insertion of the carbene in the C–H bond of the substituent are always present in the reaction medium.

The reactions involving the addition of carbenes to carbon–heteroatom multiple bond are less familiar because diazo-compounds can add directly to the C=X multiple bonds without the intermediate formation of carbenes. Furthermore, by no means every carbene is capable of attacking such a bond (for example, triplet carbenes). In a carbon–heteroatom multiple bond the heteroatom is usually more electronegative, i.e. behaves as the nucleophilic centre of the substrate. Consequently, depending on the electrophilic or nucleophilic nature of the bivalent carbon atom, singlet carbenes can initially attack either the heteroatom or the carbon atom in the C=X bond and identical compounds are formed in both cases.

When cyclohexadienone carbenes interact with aliphatic ketones, oxaspirodienones are formed as a result of the intramolecular stabilisation of the 1,3-dipolar ion[46,47]:



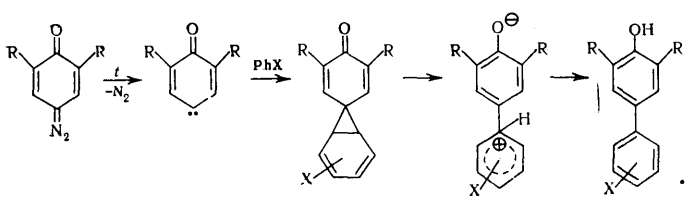
where R = $C(CH_3)_3$.

It is remarkable that oxaspirans are formed only when aliphatic ketones are used. The thermolysis of 2,6-di-t-butylbenzene 1,4-diazo-oxide in acetophenone and benzaldehyde gives rise to products resulting from insertion in the C–H bonds of the aromatic ring[47].

Interaction with Aromatic Compounds

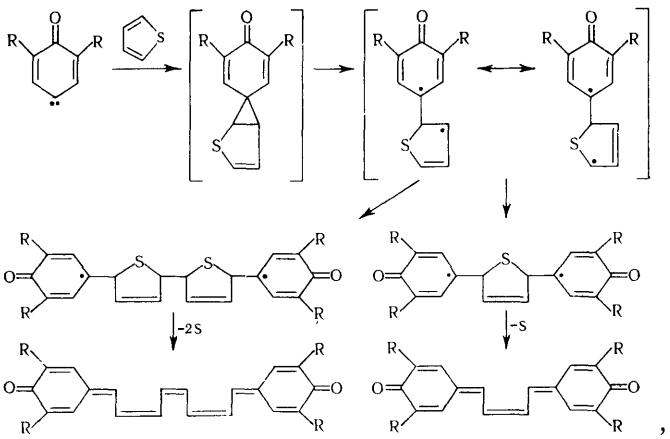
Such a reaction is characteristic of carbenes which are fairly electrophilic. It is generally accepted that it begins with attack by the carbene on the π-electron system of the aromatic compound. The further course of the reaction is determined by the stability of the intermediate norcaradiene structure. Depending on the nature of the attacking carbene, either a reversible norcaradiene–cycloheptatriene transformation is observed (the equilibrium is usually displaced towards the formation of the cycloheptatriene) or the norcaradiene structure is aromatised with formation of the formal product of insertion in the C–H bond of the aromatic ring. The latter process is more characteristic of cyclic carbenes with a π-electron system[48,49].

When cyclohexadienone carbenes interact with benzene derivatives, the main products are 4-arylphenols[50–59]. It is interesting that, when benzene derivatives are used, a mixture of isomeric 4-arylphenols is produced[55–57]. A number of investigators[51,55–58] observed the so called alcohol effect, which consists in an increased yield of 4-arylphenols when small amounts of alcohols are added to the aromatic substrate. The observed effects are explained satisfactorily by the reaction mechanism proposed by Dewar and Narayamaswami[57]:



The formation of the thermally unstable norcaradiene, which rearranges to the formal product of insertion in the C–H bond, constitutes an intermediate stage. The increase of the yield of 4-arylphenols following the addition of an alcohol is evidently associated with the increase of the lifetime of the singlet carbene owing to its stabilisation on formation of complexes with alcohol molecules. It is noteworthy that all attempts to detect the formation of the intermediate norcaradiene were unsuccessful[59]. However, the available experimental data show that the proposed reaction mechanism is the most likely.

This has been confirmed by studies on the interaction of cyclohexadienone carbenes with pyridine[51], thiophen[60,61], furan[62], and *N*-methylpyrrole[63]. In all cases the products are formed as a result of the addition of the singlet carbene to the multiple bonds of the substrate. The studies of the reactions with thiophens are the most interesting in this respect[60,61]:

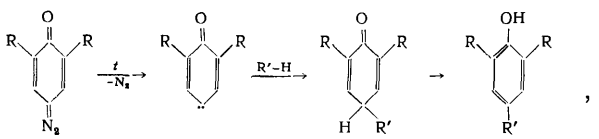


where R = $C(CH_3)_3$.

The reaction is accompanied by the formation of products not containing sulphur. Their composition can be satisfactorily accounted for by the above mechanism involving the formation of a spirodienone—the product of the addition of the carbene to a multiple bond of the thiophen.

Interaction with Hydrocarbons and Halogenohydrocarbons

The thermal decomposition of 2,6-di-t-butylbenzene 1,4-diazo-oxide in saturated cyclic hydrocarbons leads to 4-cycloalkylphenols. Their formation can be represented as a result of direct insertion of the cyclohexadiene carbene in the C–H bond of the hydrocarbon, resulting in the initial formation of an unstable quinolid compound, which readily isomerises to the phenol[54,64]:



where R = $C(CH_3)_3$. The absence of chemical polarisation in the phenol shows that the main process proceeds via a non-radical mechanism.

When alicyclic hydrocarbons are used in the reaction, a mixture of phenols is formed[64]. The low selectivity of the insertion reaction ($2^0 : 1^0 = 3.3$) is consistent with the hypothesis of the direct insertion of the singlet form of

the carbene in a C–H bond of the hydrocarbon. One should note that the reaction mixture contains stable compounds of the quinolid type, the formation of which can be accounted for by the partial transition of the carbene to the triplet state.

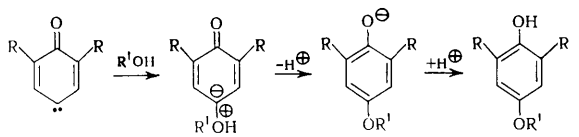
The reaction of cyclohexadienone carbenes with halogenohydrocarbons has provided wide possibilities for the synthesis of cyclohexadienone compounds, in which one of the geminal substituents is a halogen[29-31,65-67]. The interest in this reaction is due to the unusual mechanism of the insertion of carbenes in the carbon–halogen bond. In a series of studies, the reactions of cyclohexadienone carbenes with halogenohydrocarbons have been accounted for by an ylid mechanism[54,65]. The isolation of the intermediate ylid in the photolysis of 2,6-di-t-butylbenzene 1,4-diazo-oxide in 4-bromo-2,6-diazopropylphenol is quoted in support of this. The formation of side products is attributed to the $S \rightarrow T$ transition of the carbenes. However, as shown above, the $S \rightarrow T$ transition of cyclohexadienone carbenes is observed only in exceptional cases.

CIDNP data[29-31] showed that the process proceeds via a radical mechanism. The composition of the final products of the reaction of cyclohexadienone carbenes with halogenohydrocarbons is determined by their structure and the nature of the halogen. Thus, when carbon tetrachloride is used as the solvent, the main reaction product is a quinochloride. The replacement of one chlorine atom in CCl_4 by bromine or hydrogen leads to a complex composition of the reaction products[66]; nevertheless their formation is satisfactorily accounted by a radical mechanism.

Insertion in the O–H and C–O Bonds

Cyclohexadienone carbenes are electrophilic species and should therefore add to the lone electron pairs of heteroatoms with formation of intermediate ylid structures. From this standpoint, the mechanism of their insertion in the O–H and C–O bonds should be unique.

The study of the thermolysis and photolysis of benzene 1,4-diazo-oxide in aqueous[68], alcoholic[50,69], and acid media[69] showed that the main reaction products are the corresponding hydroquinones and the ethers and esters derived from them:



The main reaction is as a rule accompanied by radical side processes involving the dehydrogenation of the substrate and the formation of products derived from the phenoxy-radicals.

The composition of the products of the reaction of cyclohexadienone carbenes with the C–O bond of ethers depends on the structure of the initial arene diazo-oxide. Thus thermolysis of the unsubstituted arene diazo-oxide and of its dimethyl derivatives in tetrahydrofuran yields a mixture of high-molecular-weight products in which the arene diazo-oxide and ether fragments alternate[52,53]. On the other hand, in the thermolysis of 2,6-di-t-butylbenzene 1,4-diazo-oxide the main products are quinol spiro-ethers[70].

The characteristics of the electronic structure, the multiplicity of energy states, and the reactivity of cyclohexadienone carbenes discussed here show that carbenes of this type differ significantly from other bivalent carbon derivatives. Cyclohexadienone carbenes constitute an extremely convenient model for the investigation of the mechanisms of reactions involving the intermediate formation of methylene. The simplicity of the identification of the final products of their reaction with the substrate is of interest in connection with the development of methods for the determination of the multiplicity of the energy states of reacting carbenes. Finally, many of the reactions can be used successfully for the preparative synthesis of substituted phenols and their quinolid and spiran derivatives.

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The Structure and Reactivity of 3-Hydroxypyridine Derivatives in Electrophilic Substitution

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The structure and reactivity of 3-hydroxypyridine and its derivatives in electrophilic substitution are considered and the problems concerning the mechanism and direction of electrophilic substitution in 3-hydroxypyridines are discussed as a function of the type of reaction, its conditions, and the nature of the substituent in the 3-hydroxypyridine ring. The reactivities of 3-hydroxypyridines are compared with the results of theoretical calculations by the Hückel molecular orbital and the Pariser - Parr - Pople method. Data for the biological activities of various 3-hydroxypyridine derivatives are presented.
The bibliography includes 117 references.

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I. INTRODUCTION

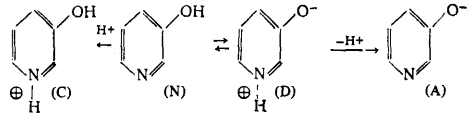
The number of studies dealing with the search for physiologically active compounds based on biogenic antioxidants has greatly increased in recent years. Academician N. M. Emanuel''s concept of the possibility of suppressing by non-toxing inhibitors undesirable free-radical reactions occurring in the organism in pathological states, in particular during malignant growth, radiation sickness, stress phenomena, and ageing, has served as a basis for the medico-biological application of these compounds[1-3]. Emanuel' suggested that phenol and polyphenol derivatives are suitable as inhibitors for this purpose. Numerous studies on the biological activity of these compounds showed that they exhibit pronounced antitumour properties and confer protection from radiation[4-6]. This stimulated further development of synthetic studies in this field. The structural difference between a number of the most effective phenolic antioxidants and the fragments of biochemical systems involved in cell metabolism, as a result of which the former are hydrophobic and possess a number of other undesirable properties, constituted an obstacle to their application in biology. In the attempts to overcome these obstacles, several ways were proposed for the synthesis of new phenolic compounds transformed as a result of the mono- and di-*ortho*-screening of the hydroxy-group. Substituted *p*-hydroxyphenylanilines, their decarboxylation products (tyramines and epinines) related to the alkaloid mescaline, *p*-hydroxybenzylamines structurally related to the precursor of the alkaloid capsaicin, and a number of arylaminobutyric acids and pyrrolidinones have been synthesised[7-10]. However, the amino-group, which ensures hydrophilic properties is as a rule also responsible for an increase in toxicity.

In order to find effective biogenic inhibitors, we undertook a study of heterocyclic hydroxy-derivatives. We chose for investigation 3-hydroxypyridine derivatives, the inhibiting properties of which might be due to the presence of the phenolic hydroxyl next to the conjugated cyclic bond system, and their structural similarity to compounds of the vitamin B_6 group (pyridoxine, pyridoxamine, and pyridoxal) ensured that the preparations synthesised were biogenic. Furthermore, the presence of the ring nitrogen atom together with the hydroxy-group made it possible to obtain water-soluble compounds as a result of salt formation. The synthesis of a large number of non-toxic and water-soluble inhibitors with biological activity was based on electrophilic reactions of 3-hydroxypyridine and its derivatives.

Attention is therefore concentrated in the present review on the characteristics of the structure and reactivity in electrophilic substitution of 3-hydroxypyridine and its derivatives.

II. ELECTRONIC STRUCTURE OF 3-HYDROXYPYRIDINE AND ITS DERIVATIVES

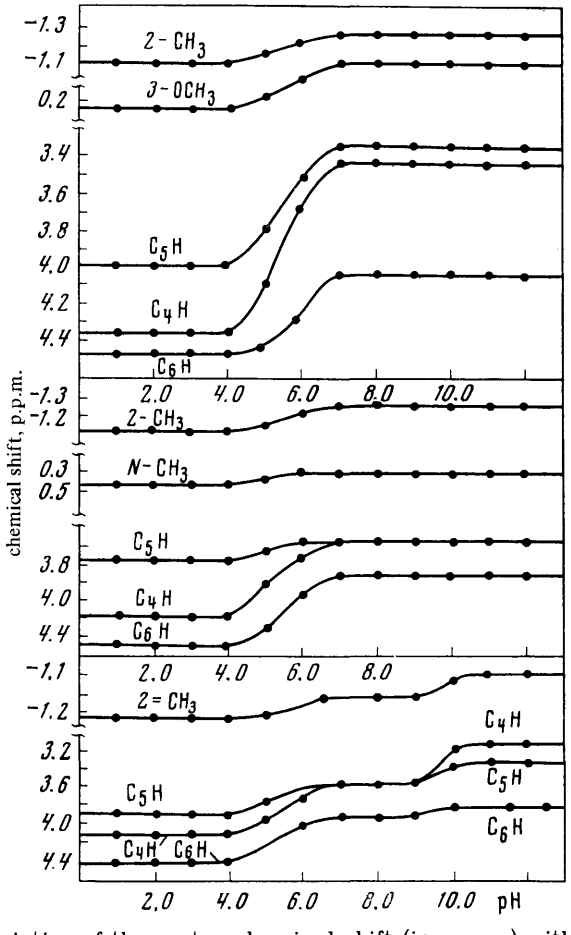
One of the characteristics of the 3-hydroxypyridine molecule, in contrast to aromatic phenols, is its ability to exist in four forms as a function of the pH of the medium: neutral (N), dipolar (D), cationic (C), and anionic (A), which is clearly reflected in the physicochemical properties and chemical behaviour of 3-hydroxypyridines in electrophilic substitution:



The presence of the dipolar form in a neutral medium was established by ultraviolet spectroscopy[11,12], potentiometric titration[13-15] as well as infrared spectroscopy and ^1H NMR.[16-18] It has been shown that in D_2O solution there is 54% of form (D) and 46% of form (N), while in pure dioxan form (D) is virtually absent[11].

The introduction of an alkyl, benzyl, or phenyl group into the 3-hydroxypyridine molecule does not decrease the possibility of the formation of all four forms. On the

contrary, the formation of the *N*-oxide of 3-hydroxypyridine has a significant influence on the acid–base equilibrium. The absence of form (D) of 3-hydroxypyridine *N*-oxide and a number of its derivatives in a neutral aqueous solution has been demonstrated by ultraviolet spectroscopy[19-20]. The limits of the existence of forms (A), (D), (N), and (C) of 3-hydroxypyridine and its derivatives were studied by ^{1}H NMR [18,21-22]—by investigating the dependence of the chemical shifts of the 3-hydroxypyridine ring protons on the pH of the medium†. The presence of three horizontal sections corresponding to the acid, neutral, and alkaline media (see Figure) has been noted and it has been shown that the ring nitrogen is fully protonated at pH < 4 and the ionisation of the OH group terminates at pH > 10.



Variation of the proton chemical shift (in p.p.m.) with the pH of the medium for different 3-hydroxypyridine derivatives: *a*) 3-hydroxy-2-methylpyridine; *b*) 3-hydroxy-2-methylpyridinium methiodide; *c*) 3-methoxy-2-methylpyridine.

† The results obtained for 3-hydroxy-2-methylpyridine are quoted as an example. The findings obtained for a large number of related compounds are similar.

The curves for aminomethyl derivatives of 3-hydroxypyridine in an acid medium have two horizontal sections due to the possibility of the protonation of two centres: the ring nitrogen and the nitrogen in the side chain.

The electronic structure of 3-hydroxypyridine has been the subject of a detailed study using quantum-chemical calculations and ^{1}H NMR data. Calculations of the electronic structure parameters of 3-hydroxypyridine [the energy of π-electron delocalisation E_π^d, the energies of the highest occupied and lowest vacant molecular orbitals (HOMO and LVMO), and the energy differences ΔE between them, the electronic charges, and bond lengths] were performed using the simple and extended molecular orbital methods[23-25] as well as the Pariser–Parr–Pople method[26]. The calculated values of E_π and E_π^d of forms (N), (A), (D), and (C) differ comparatively little from one another (Table 1). As was to be expected, the values of E_π^d for the forms containing exocyclic anionic oxygen are somewhat higher than for the hydroxy-forms.

Table 1. The energy characteristics of the electronic structure of 3-hydroxypyridine.

Form	E_π	E^d	E_{HOMO}	E_{LVMO}	ΔE
Neutral	11.975	1.917	0.564	0.894	1.458
Dipolar	10.960	2.199	0.459	0.785	1.244
Anionic	10.438	2.169	0.487	0.894	1.381
Cationic	12.482	1.988	0.630	0.786	1.416

The interaction of exocyclic oxygen with the pyridine ring is indicated by the C–O bond order, which is 0.295–0.394, and the π-electronic charge (+0.082–+0.146). The conjugation of the oxygen in the anionic form is much more marked than that of the hydroxyl oxygen: the PyC–O$^-$ bond order is 25% greater than the PC–OH bond order and the π-electronic charge on the anionic oxygen is almost twice as high as on the phenolic oxygen. The conclusion that the exocyclic oxygen interacts with the aromatic ring agrees with X-ray diffraction data, according to which the C–O bond length in phenol derivatives (1.37 Å) is smaller by approximately 0.1 Å than in saturated compounds (1.47 Å).[27] The calculated bond orders in the pyridine ring are high and similar, which may be attributed to the high degree of aromaticity of the ring and equalisation of its bonds. The interatomic distances in the four forms of 3-hydroxypyridine agree well with the available experimental lengths of the C⋯C bonds in benzene (1.397 Å), the C–N bonds in pyridine (1.34 Å), and the C–O bonds in phenols (1.37 Å) as well as the bond lengths in the ring of nicotinic acid as a model compound[28]: r_{CN} = 1.34 Å and r_{CC} = 1.39 Å.

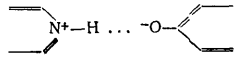
The π-electron density distribution in the 3-hydroxypyridine ring is non-uniform largely because of the presence of the ring nitrogen atom and the exocyclic oxygen atom. In consequence of the high electronegativity of the nitrogen atom (3.0) compared with that of carbon (2.5), a considerable negative π-electronic charge (–0.192) is concentrated on the nitrogen atom of the phenolic and anionic forms. As was to be expected, protonation of the nitrogen atom leads to a marked increase of the negative π-electronic charge on the nitrogen atom (–0.394) and its corresponding decrease on the carbon atoms.

Quantum-chemical calculations by the Pariser–Parr–Pople method were also used for a quantitative interpretation of the electronic absorption spectra of 3-hydroxypyridine[29,30]. All the observed absorption bands were assigned to $\pi-\pi^*$ transitions. A satisfactory correlation has been observed between the calculated and experimental absorption bands for both neutral and anionic forms.

The influence of the substituent on the electronic structure of the 3-hydroxypyridine ring was studied by ^{1}H NMR and quantum-chemical calculations of the electronic structure of alkyl and aminomethyl derivatives of 3-hydroxypyridine[23]. The distribution of electron density in the 3-hydroxypyridine ring was found to have the following characteristics.

1. In an inert medium the electron density at the carbon atoms increases in the sequence $C_{(6)} < C_{(2)} < C_{(4)} < C_{(5)}$.
2. In an aqueous medium the sequence remains the same.
3. In an alkaline medium the electron density increases in the sequence $C_{(5)} < C_{(6)} < C_{(2)} < C_{(4)}$, while in an acid medium the sequence becomes $C_{(4)} < C_{(6)} < C_{(2)} < C_{(5)}$.
4. On passing from inert and aqueous media to an acid medium, the electron density at the carbon atoms diminishes, the decrease becoming more pronounced in the sequence $C_{(5)} < C_{(2)} \leq C_{(6)} < C_{(4)}$.
5. On passing from an inert to an alkaline medium, the electron density increases. The most marked increase is observed for $C_{(6)}$ and then for $C_{(2)}$, $C_{(4)}$, and $C_{(5)}$.

Comparison of the experimental data for an inert medium with the charges calculated by the LCAO-MO method showed that the best agreement is achieved with the results of calculations for molecules in an uncharged form, where the charge increases in the sequence $C_{(6)} \leq C_{(2)} < C_{(4)} < C_{(5)}$. The calculation for the dipolar form led to another sequence: $C_{(4)} < C_{(6)} < C_{(5)} < C_{(2)}$, which agrees well with the sequence of the chemical shifts calculated for the dipolar form in an aqueous medium. This shows that in solutions in inert solvents (dimethyl sulphoxide and dioxan) the 3-hydroxypyridine molecules exist mainly in the uncharged form. However, in concentrated solutions, association complexes of the type



may make a major contribution in view of the existence of powerful intermolecular hydrogen bonds.

Direct comparison of the chemical shifts and the calculated charges for the entire series of test compounds revealed a very approximate agreement. The reason for the observed discrepancy is, apart from the approximate nature of the Hückel method, the influence on screening by factors such as dipole moments and the anisotropy of the diamagnetic susceptibility of the C–N, C–O, C–CH_3, and other bonds. However, in calculations on the electronic structure of 3-hydroxypyridine by the extended Hückel method[25] a satisfactory agreement was obtained between the chemical shifts and the calculated charges in the above series of compounds. Since the mode of electrophilic substitution reactions of heterocyclic compounds is determined by the state of the electron cloud in the molecule, as for aromatic compounds, the application of the molecular orbital theory made it possible to predict the substitution sites in the pyridine series and its derivatives. The reactivity indices for 3-hydroxypyridine were calculated both for the isolated molecule (π-electron densities, boundary electron densities, free valence index) and the reacting molecule (localisation energy) approximations[24]. Analysis of the calculated reactivity indices of 3-hydroxypyridine in the four forms (A), (D), (N), and (C) showed that the best agreement with experiment is observed for the localisation energies L_e. According to the values of L_e, electrophilic attack on the 3-hydroxypyridine molecule in acid and alkaline media should occur in the sequence $C_{(2)} > C_{(6)} > C_{(4)}$. Comparison of the values of L_e for forms (A) and (C) indicates a greater reactivity of the former.

III. ELECTROPHILIC REACTIONS OF 3-HYDROXYPYRIDINE DERIVATIVES

1. Acid- and Base-catalysed Deuterium Exchange

The electrophilic deuteration reaction of nitrogen-containing heterocycles has been widely used to elucidate the mechanism of electrophilic substitution in these compounds and also to obtain a quantitative estimate of the influence of the ring nitrogen and of a wide variety of functional substituents on the reactivity of the heteroaromatic ring[31–37].

Acid-catalysed deuterium exchange involving 3-hydroxypyridine and its alkyl derivatives made it possible to determine the sequence and rates of substitution of various positions in the 3-hydroxypyridine ring[38]. It was found that the 2-position is the most reactive while the 4-position is the least reactive. The introduction of the *N*-oxide group greatly increases the reactivity of the 2-position. For example, it has been shown[33] that 3-hydroxypyridine *N*-oxide is deuterated in the 2-position in the uncharged form, whereas both 3-hydroxy- and 3-methoxy-pyridines are not involved in the exchange under analogous conditions. On the other hand, 3,5-dimethoxypyridine *N*-oxide enters into the exchange reaction and both the 2- and 6-positions in the neutral or protonated form are involved, depending on the acidity of the medium. The ratio of the rates of deuterium exchange involving the uncharged and protonated forms is 1000, which constitutes an excellent demonstration of the powerful deactivation of the pyridine ring on protonation of the ring nitrogen.

On passing from acid-catalysed to base-catalysed deuterium exchange involving 3-hydroxypyridine, there is an appreciable increase of the rate of exchange of the protons of the 3-hydroxypyridine ring, probably owing to the involvement of the latter in this type of substitution in the most reactive anionic form[39,40]. In contrast to acid-catalysed deuterium exchange, where the exchange of the 3-hydroxypyridine ring protons was not observed, in the base-catalysed process the $H_{(2)}$, $H_{(6)}$, and $H_{(4)}$ protons may be exchanged, depending on the conditions (Table 2). The introduction of the CH_3 group in the 2-position and particularly in the 6-position increases the reactivity of the 3-hydroxypyridine ring[39].

Comparison of the rate constants for the exchange of the ring protons of 3-hydroxypyridine and its *N*-oxide (Table 2) shows that the introduction of the *N*-oxide group also accelerates proton exchange in the sequence $H_{(2)} > H_{(6)} > H_{(4)}$. A similar behaviour was likewise observed when deuterium-exchange data were compared for 3-hydroxy-2-methylpyridine and its *N*-oxide[40]. Comparison of the results for base-catalysed deuterium exchange involving 3-hydroxypyridine and its derivatives established that the rate of exchange of the $H_{(2)}$ proton is higher by an order of magnitude than the rate of exchange of the $H_{(6)}$ proton and higher by approximately two orders of magnitude than the rate of exchange of the $H_{(4)}$ proton.

2. Nitration

The hydroxy-group facilitates substitution in the pyridine ring. In contrast to pyridine, the nitration of hydroxypyridine proceeds smoothly and in high yields. Nitration of 3-hydroxypyridine proceeds exclusively in the 2-position. 3-Hydroxypyridine reacts in the protonated form[41]. The first study of the nitration of 3-hydroxypyridine was carried out by Plazek and Rodgwald[42], who obtained 3-hydroxy-2-nitropyridine and demonstrated its structure by a series of chemical transformations. In a later investigation the 6-nitro-isomer was obtained in a negligible yield (1%) together with the 2-isomer (74%):[43]

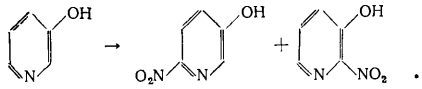
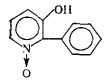
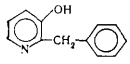
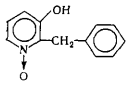
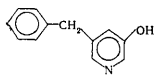
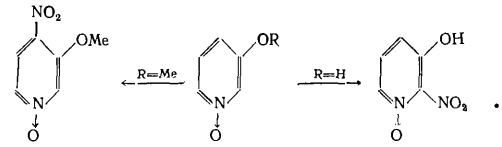


Table 2. The rate constants for the base-catalysed deuterium exchange involving 3-hydroxypyridine, its 2-methyl, 2-phenyl, 2-benzyl, and 5-benzyl derivatives, and their *N*-oxides at 160°C in 0.5*N* NaOD solution[40].

Compound	k_2, min^{-1}	k_6, min^{-1}	k_4, min^{-1}
	$1.1\cdot10^{-2}$	$1.2\cdot10^{-3}$	$5.1\cdot10^{-4}$
	$2.3\cdot10^{-2}$	$2.5\cdot10^{-3}$	$9.0\cdot10^{-4}$
	—	$3.7\cdot10^{-3}$	—
	—	$6.0\cdot10^{-3}$	$1.6\cdot10^{-3}$
	—	—	$7.8\cdot10^{-4}$
	—	$1.6\cdot10^{-3}$	$1.5\cdot10^{-3}$
	—	$4.6\cdot10^{-3}$	$1.0\cdot10^{-3}$
	$7.1\cdot10^{-3}$	$1.5\cdot10^{-3}$	$6.0\cdot10^{-4}$

Such selective substitution in the 2-position of the 3-hydroxypyridine ring is probably caused by the significant influence of the six-membered chelate complex of the hydroxy-group and the nitronium ion, formed in the transition state, on the site of substitution[44].

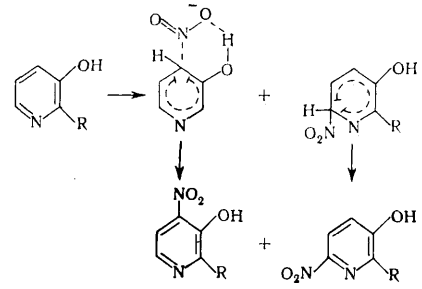
3-Hydroxypyridine *N*-oxide is nitrated similarly in the 2-position, which indicates a more powerful directing effect of the 3-hydroxy group than the *para*-directing effect of the *N*-oxide group[45]:



On the other hand 3-alkoxypyridine *N*-oxides are nitrated exclusively in the 4-position[46,47], which shows that the *para*-directing influence of the *N*-oxide group predominates.

In contrast to the base *N*-oxide, 3-methoxy-[48,49] and 3-ethoxypyridines[50] give rise to the 2-nitro- and 2,6-dinitro derivatives depending on the experimental conditions. 3,5-Diethoxypyridine *N*-oxide is also nitrated in the 2- and 6-positions instead of the expected 4-position[51,52].

Very interesting results were obtained in the nitration of 2-alkyl- and 2-chloro-3-hydroxypyridines[49,53]. It was found that in this case the 4-position as well as the 6-position is nitrated, the formation of the 4-isomer predominating[44]:



The authors suggested that the preferential nitration in the *ortho*-position relative to the hydroxyl in these compounds is due to the formation of a six-membered chelate complex in the transition state. This hypothesis is confirmed by the finding that, when the nitration is carried out at a higher temperature, which weakens the intramolecular hydrogen bond, the 6-position is preferentially substituted. On the other hand, nitration of 3-methoxy-2-methylpyridine, which cannot form a hydrogen bond with the attacking nitronium ion, proceeds exclusively in the 6-position.

The occurrence of 6-substitution only in the nitration of 3-hydroxy-2-nitropyridine can also be a consequence of the impossibility of the formation of a chelate when the nitronium ion attacks the 4-position because of the strong intramolecular hydrogen bond between the nitro- and hydroxy-groups already present in the compound. The influence of chelate formation on the direction of substitution has been confirmed also in the nitration of the *N*-oxides of 3-hydroxy-2-methyl- and 3-methoxy-2-methyl-pyridines[54,55]. The nitration of 3-hydroxy-2-methylpyridine *N*-oxide is directed exclusively to the 4-position, while 3-methoxy-2-methylpyridine is nitrated in the 6-position.

It is interesting to note that the nitration of 3-methoxy-6-methylpyridine[56] proceeds in the 2-position, in contrast to 3-methoxypyridine, while 3-hydroxy-2-methoxypyridine is nitrated exclusively in the 4-position. As expected, the nitration of 3-hydroxy-6-methyl- and 3-hydroxy-4-methyl-pyridines is directed to the 2-positions[57].

The presence of the nitro-group in the 3-hydroxypyridine ring does not preclude its further nitration. Thus nitration of 3-hydroxy-6-methyl-2-nitro- and 3-hydroxy-2-methyl-6-nitro-pyridines yielded the corresponding dinitro-derivatives[57]. Nitration of 3-hydroxy-2-nitropyridine results in the formation of 3-hydroxy-2,4,6-trinitropyridine together with the 2,6-dinitro-derivative[58]. When the 2- and 6-positions of the 3-hydroxypyridine ring were occupied by alkyl groups, the 4-position was substituted smoothly[57,59]. Thus the results presented indicate the possibility of the successive selective nitration of the 2-, 6-, and 4-positions of the 3-hydroxypyridine ring.

To elucidate the mechanism of the electrophilic substitution of the 3-hydroxypyridine ring, the kinetics of the nitration of 3-hydroxypyridine were studied[41]. Comparison of the variation of the rate of nitration with pH for 3-hydroxy- and 3-methoxy-pyridines with the results found previously for the 2,4,6-collidinium cation revealed their considerable similarity, which suggested the involvement of the 3-hydroxypyridine ring in nitration in the protonated form. The partial rate factors in the nitration of the 3-methoxypyridinium cation are 4×10^{-10} for the 2-position and 1×10^{-11} for the 6-position.

3. Halogenation

The halogenation of 3-hydroxypyridine has been studied in detail in many investigations. It has been shown that substitution proceeds primarily in the 2-position. Bromination with an equivalent amount of bromine in pyridine[60], iodination with iodine in sodium carbonate solution[61,62], and chlorination with hydrochloric acid in the presence of hydrogen peroxide[61] all lead to the formation of 2-halogeno-derivatives. The 4- and 6-halogeno-derivatives of 3-hydroxypyridine has been obtained only by an indirect procedure[60].

The iodination of 3-hydroxypyridine with an excess of iodine proceeds with formation of 2,6-diiodo- and 2,4,6-triiodo-derivatives[61]. Under these conditions, 3-hydroxy-5-methylpyridine gives rise to the 2,6-diiodo-derivative[63]. Similarly the bromination of 3-hydroxypyridine with twice the molar amount of bromine in pyridine yields the 2,6-dibromo-derivative and the reaction with an excess of bromine water results in the formation of 2,4,6-tribromo-3-hydroxypyridine[60]. The bromination of 5-bromo-3-hydroxypyridine with an excess of bromine water yielded 2,4,5,6-tetrabromo-3-hydroxypyridine[60].

The bromination of 3-hydroxypyridine *N*-oxide, like that of the non-oxidised base, leads to the 2-bromo-derivative, which can be brominated further to give the 2,6-dibromo- and 2,4,6-tribromo-3-hydroxypyridine *N*-oxides[64]. In contrast to this, the iodination of 3-hydroxypyridine *N*-oxide in a weakly alkaline solution leads to the formation of 3-hydroxy-4,6-diiodopyridine *N*-oxide as the only product[65]. The bromination of 3,5-diethoxypyridine in an acid medium results in the formation of 2,6-dibromo-3,5-diethoxypyridine, while in pyridine solution the main product isolated was 2-bromo-3,5-diethoxypyridine[66]. 2,3,4-Trihydroxypyridine gives rise to a monohalogeno-derivative of unknown structure[67].

The introduction of the electronegative nitro-group does not affect the halogenation process; the bromination of 3,5-diethoxy-2-nitropyridine yields 6-bromo-3,5-diethoxy-2-nitropyridine[66]. The iodination of 3-hydroxypicolinic acid with iodine in an alkaline medium proceeds with simultaneous decarboxylation and the formation of 3-hydroxy-2,6-diiodopyridine[68].

4. Sulphonation

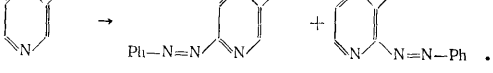
The sulphonation of 3-hydroxypyridine requires the use of extremely severe conditions and proceeds with formation (in a low yield) of 3-hydroxypyridine-2-sulphonic acid[69,70]. Similarly 3-hydroxypyridine *N*-oxide is sulphonated in the 2-position[71]. Comparison of the conditions for the sulphonation of pyridine and 3-hydroxypyridine indicates a lower reactivity of the latter in this reaction.

It has been suggested[71] that the sulphonation of pyridine and its derivatives proceeds via the initial formation of a complex of sulphur trioxide with the heterocycle, which rearranges to the corresponding sulphonic acid at a high temperature in the presence of catalysts. The rate-determining state of the reaction is the rearrangement of the complex, the ease of which is determined by the stability of the heterocycle–sulphur trioxide complex formed. The higher stability of the complex of 3-hydroxypyridine with sulphur trioxide compared with that formed by pyridine itself is probably the cause of its lower reactivity in sulphonation.

5. Azo-Coupling

The azo-coupling of 3-hydroxypyridine proceeds preferentially in the *para*-position relative to the hydroxy-group. Thus the main product formed in the interaction with benzenediazonium chloride is 3-hydroxy-6-(phenylazo)-pyridine (81%) together with a small amount (3%) of the 2-isomer[72].

On the other hand, the reaction of 3-hydroxypyridine with *p*-nitrobenzenediazonium chloride in a weakly acid solution led initially to the isolation of only the 2-azo-derivative[62]. Later studies demonstrated the formation of equal amounts of 2-azo- and 6-azo-derivatives[73]. On the other hand, when the above reaction was carried out under weakly alkaline conditions, the preferential formation of the *para*-isomer was observed; the yield of the *ortho*-isomer was 13% under these conditions:



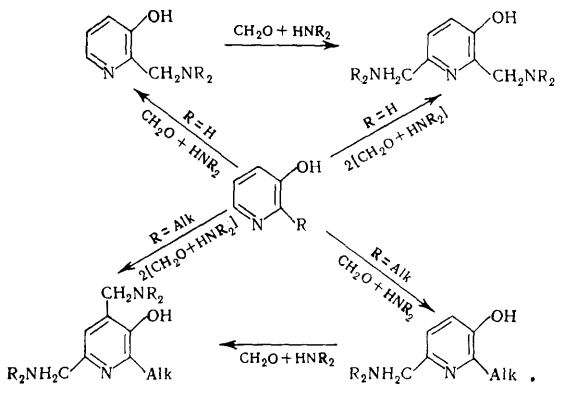
The azo-coupling of 3-hydroxypyridine *N*-oxide in a weakly alkaline solution, like that of 3-hydroxypyridine itself, involves the 6-position[74]. The azocoupling of 3-hydroxy-4-methyl-5-phenylpyridine with benzenediazonium chloride gives rise to a mixture of equal amounts of the *o*-azo- and *p*-azo-derivatives[73]. The azo-coupling of 3-hydroxy-2-methyl- and 3-hydroxy-6-methylpyridines and their *N*-oxides proceeds with formation of only the 6-azo- and 2-azo-derivatives respectively[75]. The absence of 4-substitution proved to be general in the azo-coupling of both the 2- and 6-methyl derivatives and of the 2,6-dimethyl derivatives of 3-hydroxypyridine with benzene-diazonium chloride[75]. However, the introduction of the *N*-oxide group permitted a smooth azo-coupling in the 4-position of 3-hydroxy-2,6-dimethylpyridine *N*-oxide[74].

The azo-coupling of 2,3-dihydroxypyridine, 3-hydroxy-2-methoxypyridine, and 3-hydroxy-1-methyl-2-pyridone involves the 6-position[76]. This shows that the main directing group in all the compounds is the 3-hydroxy-group. The decisive directing influence of the 3-hydroxy-group was established also in the azo-coupling of 2,5-dihydroxypyridine, which involves the 6-position[76].

6. Aminomethylation

3-Hydroxypyridine in the anionic form enters into a number of reactions with weak electrophilic agents, which are characteristic of phenolic compounds. Among these one must include the aminomethylation, hydroxymethylation, and carboxylation reactions. The aminomethylation of 3-hydroxypyridine and its derivatives has been studied both with the aim of synthesising pyridoxine (vitamin B_6),[77] its analogues[78], and antagonists[79] and with the aim of studying the comparative reactivities of the 2-, 4-, and 6-positions in the 3-hydroxypyridine ring.

The pronounced electron-accepting influence of the ring nitrogen, which greatly reduces the electron density in the aromatic ring, particularly in the 2-, 4-, and 6-positions, leads to a reduced reactivity of 3-hydroxypyridine in the Mannich condensation compared with phenols. Thus, in contrast to phenol, which readily gives rise to a trisubstituted Mannich base, 3-hydroxypyridine is aminomethylated only in the 2- and 6-positions[80]. Furthermore, the combination in a single molecule of the hydroxy-group adjoining the conjugated ring system with the ring nitrogen atom alters the sequence of substitution from *ortho-ortho-para*, as in phenols, to *ortho-para-ortho* in 3-hydroxypyridine:



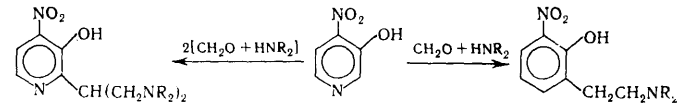
The success of the aminomethylation depends markedly on the pH of the medium[81]. Whereas phenols are readily aminomethylated in both acid and weakly alkaline media, the maximum yield of Mannich bases formed from 3-hydroxypyridines is achieved in weakly alkaline media. The different reactivities of the 2-, 6-, and 4-positions of the 3-hydroxypyridine ring in the Mannich condensation make it possible to synthesise the individual compounds. Both 2-dialkylaminomethyl- and 2,6-bis(dialkylaminomethyl)-3-hydroxypyridine can be readily obtained from 3-hydroxypyridine[80]. The mode of reaction can be controlled by an appropriate choice of reactant ratio. However, in all stages there is an initial attack on the 2-position and then on the 6-position. Under analogous conditions, 2-alkyl-3-hydroxy-[82] and 3-hydroxy-6-methylpyridines[80] are aminomethylated with formation of the corresponding 6- and 2-dialkylaminomethyl derivatives.

4-Aminomethylation is possible only for 3-hydroxypyridines containing an alkyl or alkoxy-group in the 2-position and in many instances requires the use of more severe conditions. 2,6-Dialkyl-4-dialkylaminomethyl-3-hydroxypyridine[83], 2-alkyl-3-hydroxypyridine[82,84], and 4,6-bis(dialkylaminomethyl)-3-hydroxy-2-methoxypyridine[85] were synthesised in this way. The attempt to obtain 4-substituted compounds by the aminomethylation of 6-alkyl-2-dialkylaminomethyl- and 2,6-bis(dialkylaminomethyl)-3-hydroxypyridines was unsuccessful. This led to the conclusion that the presence in the *ortho*-position with respect to the hydroxyl of a substituent forming a strong intramolecular bond with the OH group sharply reduces the reactivity of the 4-position in the Mannich condensation. It has been noted that the reduction of the acid properties of the OH group also affects the success of substitution at the $C_{(4)}$ atom[84].

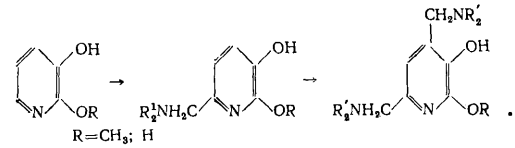
Furthermore, the course of aminomethylation is significantly influenced also by the structure of the secondary amine. Thus aminomethylation of 2,6-dialkyl-3-hydroxypyridines was unsuccessful when secondary amines such as diethylamine, diisopropylamine, and diallylamine were used, probably owing to the steric hindrance to the substitution of the 4-position[82].

The aminomethylation of 3-hydroxypyridine *N*-oxide and its 6-methoxy-2-methyl- and 2,6-dimethyl derivatives is characterised by the same sequence of the substitution of various positions of the 3-hydroxypyridine ring[86]. Comparison of the conditions for the aminomethylation of the oxidised and non-oxidised bases indicates a somewhat greater reactivity of 3-hydroxypyridine *N*-oxides[86].

Interesting results were obtained in a study of the aminomethylation of nitroderivatives of 3-hydroxypyridine. The presence of the nitro-group in the 2-position of the 3-hydroxypyridine ring does not prevent the 6-aminomethylation of 3-hydroxy-2-nitropyridine[87]. However, the aminomethylation of the 4-nitro- and 2-nitro-derivatives of 3-hydroxy-6-methylpyridine is not directed to the ring but to the side chain[88]. 2-(β-dialkylaminoethyl)-3-hydroxy-4-nitropyridines, the further aminomethylation of which leads to the formation of Mannich bis-bases via the methyl group, were synthesised in this way:



Similarly the aminomethylation of 3-hydroxy-6-methyl-2-nitropyridine yielded 6-(β-dialkylaminoethyl)-3-hydroxy-2-nitropyridines[88]. The aminomethylation of 2,3-dihydroxypyridine[89] and 3-hydroxy-2-methoxypyridine[85] leads to the initial formation of the Mannich 6-monobases and subsequently of the 4,6-bisbases, which indicates a definite role of the 3-hydroxy group in directing the substituent[85]:

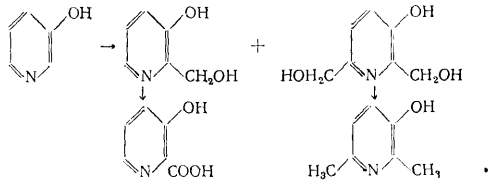


Comparison of the conditions for the aminomethylation of 2-alkyl-3-hydroxypyridines with those for 2-alkoxy- and 2-alkoxy-3-hydroxy-pyridines shows that the replacement of the alkyl group by alkoxy- and hydroxy-groups increases somewhat the reactivity of the 3-hydroxypyridine ring[85]. The aminomethylation of 3-hydroxy-1-methyl-2-pyridone proceeds, like that of 2,3-dihydroxypyridine, under mild conditions in a quantitative yield and involves the 6-position[90]. However, the attempts at 4,6-disubstitution of 3-hydroxy-1-methyl-2-pyridone were unsuccessful, which is caused, as for 3-hydroxy-2-nitropyridine and 2-dialkylaminomethyl-3-hydroxypyridine, by the presence of a strong intramolecular hydrogen bond between the 3-hydroxy-group and the *ortho*-substituent.

As in 2,3-dihydroxypyridine, the main directing group for electrophilic substitution in 2,5-dihydroxypyridine is the 3-hydroxy-group, which directs aminomethylation to the 6-position[90].

7. Hydroxymethylation

The ease of controlling the hydroxymethylation of 3-hydroxypyridine, in contrast to the rapid polymerisation of phenols under similar conditions, provide a clear example of the deactivating influence of the ring nitrogen on the chemical reactivity of the aromatic ring. 3-Hydroxypyridine can be effectively hydroxymethylated by treatment with an alkaline solution of formaldehyde[91]. This yields a mixture of mono- and di-substituted products[91,92], the formation of which cannot be avoided even when equivalent ratios of the reactants are employed[93]. The substitution of the 2-position was demonstrated by oxidising the product to 3-hydroxypicolinic acid[91] and that of the 6-position by converting the di(hydroxymethyl) compound into 3-hydroxy-2,6-dimethylpyridine[92]:



The hydroxymethylation of 3-hydroxy-2-methyl- and 3-hydroxy-6-methyl-pyridines[82,94] proceeds equally successfully with formation of the corresponding 6- and 2-isomers. 4-Substitution was not observed in either case (and also for 3-hydroxy-2,6-dimethylpyridine). The corresponding 4-hydroxymethyl derivatives of 3-hydroxy-2-methyl- and 3-hydroxy-2,6-dimethyl-pyridines were obtained indirectly from the 4-aminomethyl derivatives[82,95]. The hydroxymethylation of the 3-hydroxypyridine ring can be achieved successfully also in the presence of the electron-accepting carboxy-group in the 2-position. 5-Hydroxypicolinic acid forms the 2-hydroxymethyl derivative[96].

8. Carboxylation

Like phenol, 3-hydroxypyridine in the anionic form undergoes the Kolbe reaction with carbon dioxide under pressure. However, in contrast to phenol, the carboxylation of 3-hydroxypyridine is directed mainly to the *para*-position and not the *ortho*-position with respect to the hydroxy-group. Thus, when 3-hydroxypyridine was heated with potassium carbonate in proportions of 1 : 1.5, a quantitative yield of 5-hydroxypicolinic acid was obtained[97]. In the carboxylation of the sodium or potassium salt of 3-hydroxypyridine the formation of low yields of 3- and 5-hydroxypicolinic acids was noted, the sodium salt being substituted preferentially in the *ortho*-position and the potassium salt in the *para*-position relative to the hydroxy-group[98]. 3-Hydroxy-2-methyl-pyridine is carboxylated in the 6-position[99], while 3-hydroxy-5-methylpyridine forms an acid of unknown structure[100].

9. Other Reactions of 3-Hydroxypyridine

Other electrophilic reactions of 3-hydroxypyridine include mercuration with mercury acetate in the 2-position[101]. Vigorous attempts have been made to involve 3-hydroxypyridine in the Friedel–Krafts acylation and alkylation reactions but without success. This is probably because of the great sensitivity of these reactions to the deactivating influence of the nitrogen in the pyridine ring owing to complex formation and the corresponding change in the aromaticity of the ring. 3-Hydroxypyridine is not involved in the nitrosation reaction, which is also sensitive to the deactivating effect of electron-accepting substituents[72].

However, 2,5-dihydroxypyridine is readily nitrosated with formation of the 6-nitroso-derivative. The same position was also nitrosated in 2,5-dihydroxy-4-methyl-3-phenylpyridine[73].

IV. BIOLOGICAL PROPERTIES

3-Hydroxypyridine has been the subject of vigorous research with the aim of synthesising on its basis various biologically active compounds. Experimental studies have shown that 3-hydroxypyridine derivatives exhibit a wide spectrum of biological and pharmacological activity[102].

For example, the ethers of base-substituted 3-hydroxypyridines exhibit physostigmine-like, anticurare, and anticholinesterase activities[103]. The synthesis of a large number of 3-hydroxypyridine derivatives with bactericidal and anti-inflammatory activities has been reported[104,105]. 3-Hydroxypyridine derivatives can be used as depressants of the central nervous system[104]. Acylated 2-amino-3-hydroxypyridines have been suggested as anti-inflammatory compounds and for the treatment of cardiovascular diseases[106]. 2- and 6-Formyl-3-hydroxypyridine thiosemicarboazones exhibit a marked antileukaemic activity in both experimental and clinical tests[107]. Phosphate esters of 3-hydroxy-6-methylpyridine exhibit an insecticidal activity[108], while 3-hydroxy-2-nitropyridinium salts exhibit herbicidal activity[109]. Esters of 3-hydroxypyridines and of their nitro-derivatives have been used successfully in the synthesis of peptides and polypeptides having regular structures[110,111].

Relatively non-toxic and water-soluble radical process inhibitors with a wide spectrum of biological activity can be obtained from 3-hydroxypyridine[95]. The possibility of using inhibitors derived from 3-hydroxypyridine as agents conferring protection against radiation, discovered by Emanuel' and coworkers is of greatest interest[112,113]. 2,6-Dialkyl- and 2,4,6-trialkyl-3-hydroxypyridines exhibit the most effective anti-radiation activity. A study of the antiradiation properties of 3-hydroxypyridine derivatives and of inhibitors of other classes established a relation between the anti-radical activity of the inhibitor and its antiradiation activity[114,115]. 3-Hydroxypyridine derivatives can protect DNA molecules from radiation-induced depolymerisation[4] and also exhibit antileukaemic activity[116]. Apart from their use as prophylactic agents, alkyl-substituted 3-hydroxypyridines possess therapeutic activity against the effects of radiation and promote a more rapid recovery of the blood-forming system[116]. It has been noted that 2,6-dialkyl- and 2,4,6-trialkyl-3-hydroxypyridines possess cytogenic activity.

The mechanism of the biological action of 3-hydroxypyridine derivatives has been the subject of a detailed microbiological study on yeast cells as the biological test

object[117]. It was established that 3-hydroxypyridine inhibitors suppress the multiplication of yeast cells, which are incapable of synthesising inositol and pantothenic acid, by blocking these vitamins when the latter are introduced from outside. It has been suggested[117] that alkyl-substituted 3-hydroxypyridines function as specific inhibitors of cell division, acting primarily by arresting the division of the nuclei. It has been shown that individual alkyl-3-hydroxypyridines exhibit vitamin B_6-like activity[117].

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Thus systematic study of the structure of 3-hydroxypyridines and of their reactivity in electrophilic substitution using quantum-chemical calculations, spectroscopic methods, and the kinetics of the acid- and base-catalysed deuterium exchange made it possible to investigate the molecular sites involved in electrophilic reactions, to develop methods for the introduction of various substituents in different specific positions in the 3-hydroxypyridine ring, and to achieve on this basis the synthesis of a large number of relatively non-toxic and water-soluble inhibitors of radical chain processes with a wide spectrum of biological activity.

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Kinetic Study of the Degradation and Stabilisation of Polymers

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The kinetics and the mechanism of the thermal, thermo-oxidative, photo-oxidative, and hydrolytic degradation of polymers are surveyed. Critical phenomena in the thermal degradation of poly(vinyl chloride) are described. Specific aspects of radical reactions in the solid phase are discussed. A list of 151 references is included.

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I. INTRODUCTION

During recent years many studies have been published on the degradation and the stabilisation of polymers. The scientific and practical value of such investigation is obvious, since lengthening the life of plastic articles is equivalent to increasing the production of such articles. The summarising papers by Emanuel',[1-5] based on the application of various kinetic methods, are especially promising in the study of the mechanism of the ageing of polymers and in the search for ways of stabilising them.

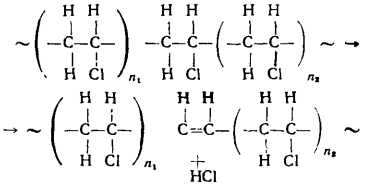
Detailed study of the kinetics and the mechanism of the degradation of polymers will permit (i) development of theoretically based accelerated methods for estimating the "lifetime" of polymers and polymeric articles under storage, processing, and service conditions, (ii) preparation of effective stabilisers for polymers and assessment of their efficiency, (iii) prolongation (or shortening†) of the useful life of polymer articles, and (iv) assessment of the effect of various additives on the stability of polymers.

Four modes of degradation of polymers—thermal, thermo-oxidative, photo-oxidative, and hydrolytic—are especially important both theoretically and practically. Overall the degradation (ageing) of polymers is a complicated radical, ionic, and molecular process involving many consecutive and simultaneous reactions.

II. THERMAL DEGRADATION

Among work on the thermal degradation of polymers a special place is occupied by studies of the degradation of poly(vinyl chloride) (p.v.c.).[6-9] This polymer is widely used in various branches of industry, but its instability when heated makes its processing and use in articles difficult.

Hydrogen chloride is evolved by the decomposition of poly(vinyl chloride):



(1)

† This is important for "one-off" uses of polymers (e.g. packaging materials) from the point of view of conservation of the environment and the regeneration of waste products.

The polymer becomes discoloured (owing to the formation of polyconjugated systems) and its physicomechanical properties change. The decomposition exhibits the principal features of a radical–chain process (rate of dehydrochlorination increased by radical initiators, and decreased by inhibitors of radical reactions)[9]. The proportionality of the rate of evolution of hydrogen chloride to the square root of the concentration of added initiators[9], indicates that destruction of the active centres involved occurs by recombination or disproportionation[7]. Degradation is initiated by the bimolecular interaction of structures P'Cl containing a labile chlorine atom with hydrogen atoms in the polymer PH to form a molecule of hydrogen chloride and two macroradicals P$^{\cdot}$ and P'$^{\cdot}$:

$$PH + P'Cl \rightarrow P^{\cdot} + P'^{\cdot} + HCl \quad . \qquad (2)$$

Molecular detachment of hydrogen chloride from the poly(vinyl chloride) molecule (reaction 1) cannot be completely excluded[7-9].

During thermal degradation in the presence of the hydrogen chloride evolved, reactions (1) and (2) are accompanied by the autocatalytic reaction

$$HCl + PH \xrightarrow{k} 2\,HCl + Pr$$

where Pr is the reaction product (macromolecules with a double bond) and k the effective rate constant. The occurrence of this reaction gives rise to critical phenomena[8,9]. The concentration of hydrogen chloride is determined in general not only by its rate of formation but also by its rate of removal from the specimen by diffusion. The variation in its concentration inside the polymer film $c(x,t)$ can therefore be described by the equation

$$\frac{dc}{dt} = D\frac{d^2c}{dx^2} + W_0 + kc,$$

where W_0 is the rate of the uncatalysed formation of hydrogen chloride, D its diffusion coefficient in the film, and k the effective autocatalysis constant. Hence the flux of hydrogen chloride through the boundary surfaces of the film ($x = 0$, $x = l$) referred to unit volume (the rate of formation of hydrogen chloride determined experimentally) can be calculated as

$$W_{HCl} = \frac{2D}{l}\frac{dc}{dx} = \sum_{n=0}^{\infty} \frac{8W_0D\left[e^{\left[k-\frac{(2n+1)^2\pi^2D}{l^2}\right]t} - 1\right]}{l^2\left[k - \frac{(2n+1)^2\pi^2D}{l^2}\right]} \qquad (3)$$

For thin films (with $\pi^2D/l^2 \gg k$ and $t > l^2/\pi^2D$) Eqn. (3) becomes

$$W_{HCl} = \frac{8W_0D}{l^2}\sum_{n=0}^{\infty}\frac{1}{\frac{(2n+1)^2\pi^2D}{l^2} - k}.$$

The rate of evolution increases as the film becomes thicker. When $\pi^2D/l^2 = k$, we have

$$W_{HCl} = \frac{8W_0Dt}{l^2},$$

i.e. W_{HCl} increases linearly with time. The presence of autocatalysis when $k > \pi^2D/l^2$ should produce an exponential increase in rate of evolution of hydrogen chloride during the process:

$$W_{HCl} = \frac{8D}{l^2}\frac{W_0e^{kt}}{k}.$$

Calculation shows [9] that at 200°C the critical film thickness (corresponding to the transition from a steady-state to an autocatalytic process) is 0.018 cm.

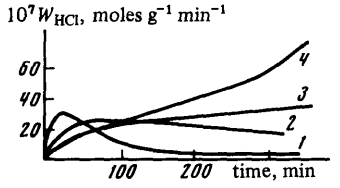


Figure 1. Rates of formation of hydrogen chloride (at 200°C) calculated by means of Eqn. (3) for poly(vinyl chloride) films of different thicknesses (mm): 1) 0.06; 2) 0.14; 3) 0.18; 4) 0.19.

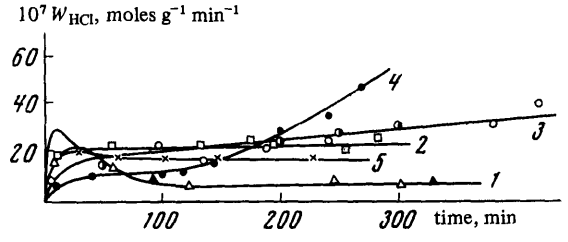


Figure 2. Rates of formation of hydrogen chloride (at 200°C) for poly(vinyl chloride) films of different thicknesses (mm): 1) 0.06; 2) 0.14; 3) 0.18; 4) 0.19; 5) finely divided powder.

Figs. 1 and 2 show good agreement between curves calculated by means of Eqn. (3), with $D = 3.3 \times 10^{-7}$ cm^2 min^{-1} and $k = 0.0103$ min^{-1}, and those obtained experimentally (at 200°C). The results demonstrate a novel type of critical phenomena in degradation processes, due to competition between catalysis by the final reaction product and its diffusion from the polymer [6-9]. It is evident from Figs. 1 and 2 that autocatalysis is absent only with very thin films and finely powdered poly(vinyl chloride). The occurrence of such critical phenomena in the thermal degradation of the polymer is the reason for the irreproducibility of the experimental results obtained by different workers.

The introduction of stabilisers to combine with hydrogen chloride (acceptors) should increase its rate of removal and hence the critical dimensions of the specimen. In the presence of an acceptor A we have

$$\frac{dc}{dt} = D\frac{d^2c}{dx^2} + W_0 + k_{eff}c,$$

where $k_{eff} = k - k_A[A]$ is the effective autocatalysis constant, k_A being the rate constant for interaction between hydrogen chloride and the acceptor, and [A] the concentration of the latter. At acceptor concentrations $[A]_{cr} \geq k/k_A$ degradation will occur under steady-state conditions whatever the size of the specimen. Taking into account the thickness of the film yields

$$[A]_{cr} = \frac{k - \frac{\pi^2}{l^2}D}{k_A},$$

i.e. the critical acceptor concentration is lower the thinner the film. This equation can be used to calculate k_A, an important quantitative parameter of hydrogen-chloride acceptors.

Thus prediction of the useful life of articles made of poly(vinyl chloride) must take into account not only the temperature and the concentration of the added stabiliser–acceptor but also the critical size of the article and the critical concentration of the stabiliser under service conditions.

III. THERMO-OXIDATIVE DEGRADATION

Significant progress in the degradation and stabilisation of polymers has recently been made particularly by kinetic investigations. The oxidation of polymers comprises in principle the same primary steps as that of simpler compounds, so that many features of their oxidation can be explained by the generally accepted scheme [10,11]. Denoting the oxidisable compound as RH (e.g. a hydrocarbon), we can write for the initial stages [10] (where R'OOR' is an initiator)

$$R'OOR' \xrightarrow{W_i} [2\,R'O'] \xrightarrow{e} R'O^{\cdot} \xrightarrow{RH} R^{\cdot};$$
$$R^{\cdot} + O_2 \xrightarrow{k_1} RO_2^{\cdot};$$
$$RO_2^{\cdot} + RH \xrightarrow{k_2} ROOH + R^{\cdot};$$
$$ROOH \xrightarrow{k_3} RO^{\cdot} + {}^{\cdot}OH;$$
$$\left.\begin{array}{l} R^{\cdot} + R^{\cdot} \xrightarrow{k_4} \\ R^{\cdot} + RO_2^{\cdot} \xrightarrow{k_5} \\ RO_2^{\cdot} + RO_2^{\cdot} \xrightarrow{k_6} \end{array}\right\} \text{Inactive products};$$

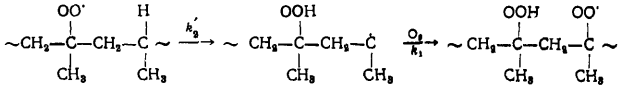
and in the presence of an inhibitor InH we have

$$RO_2^{\cdot} + InH \xrightarrow{k_7} ROOH + In^{\cdot}; \quad (4)$$
$$R^{\cdot} + InH \xrightarrow{k_7'} RH + In^{\cdot}. \quad (5)$$

However, conditions for the development of a chain reaction in a solid polymer differ markedly from those in a liquid organic compound. Recent kinetic studies of the oxidation of several (primarily carbon-chain) polymers have revealed facts that cannot be interpreted in terms of the classical scheme. Such solid-phase processes can be described quantitatively [12] by a step-by-step model of the

chain oxidation of polymers with a two-centre chain reaction and a stepwise mechanism of migration of the free valency and destruction of free radicals on collision.

According to this model the oxidation of a polymer PH involves the formation of solitary hydroperoxides POOH and adjoining peroxides $(POOH)_2$, among which the latter break down considerably more rapidly into radicals [13]. Adjacent hydroperoxy-groups are formed when a peroxy-radical attacks a β-carbon–hydrogen bond, and the resulting alkyl radical adds oxygen:



The ratio of the yields of (POOH) and $(POOH)_2$ depends on the oxygen pressure.

An important role in the mechanism of the solid-phase oxidation of polymers is played by chain-propagation reactions involving alkyl radicals‡:

$$P^{\cdot} + PH \xrightarrow{k_3''} PH + P^{\cdot},$$

which tend to move the free valency through the specimen.

As oxygen diffuses slowly and is relatively sparingly soluble in the polymer [16–20], the conversion of alkyl into peroxide macroradicals is a slow process, and the $[P^{\cdot}]/[PO_2^{\cdot}]$ ratio in the polymer is quite high, which is of great importance for solving the problem of stabilisation. Inhibitors (phenols, amines, anthracene) terminate chains in an oxidisable polymer by reacting not only with peroxide but also with alkyl radicals [21–23]. For this reason inhibitors that react mainly with alkyl radicals (iminoxyl radicals, anthracene, or quinol) inhibit the oxidation of a polymer far more efficiently than that of a hydrocarbon [23,24]. Whereas chain termination during oxidation of a polymer in solution takes place only by reaction (4), reaction (5) plays an important part in the solid polymer [25].

Thus stepwise migration of the free valency in the solid oxidisable polymer occurs by two primary processes:

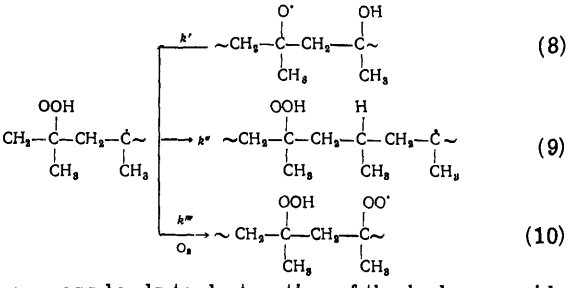
$$P^{\cdot} + PH \xrightarrow{k_3''} PH + P^{\cdot}; \qquad (6)$$

$$PO_2^{\cdot} + PH \xrightarrow{k_5} POOH + P^{\cdot}. \qquad (7)$$

During the interval between these two processes the free valency moves a distance d as a consequence of the thermal motion of the segments of the macromolecules [12]. The more mobile the segments the more rapid the migration of the active centre; the latter is determined also by the rate of the chemical reactions (6) and (7). Two such active centres are destroyed when they enter a space of $4\pi d^3/3$, where they may be brought together by the thermal mobility of the segments and interact, the rate of recombination being greater the higher the concentration of active particles, the more vigorous the movement of the segments, and the more rapid the migration of active centres through the polymer specimen [12]. The meeting of two active centres in the polymer cannot be regarded as the encounter of independent particles; k_4, k_5, and k_6 depend on the reaction conditions (pressure of oxygen, structure of polymer, solubility of oxygen, and other factors determining the composition of the radicals).

A step-by-step mechanism of migration of the free valency in the polymer predominates when the diffusion of free radicals is slow. In solution, the melt, and in the swollen polymer, where diffusion of macromolecules and their segments is facilitated, a diffusion mechanism may be a more efficient mode of migration of the free valency [26–30].

It is quite likely that, besides the "direct" step-by-step mechanism leading to formation of a block of hydroperoxy-groups on the polymer chain, $P^{\cdot}$ or $PO_2^{\cdot}$ radicals may attack hydroperoxy-groups that have just been formed [31,32]. Results obtained for the oxidation of isotactic polypropylene—a low yield of stable hydroperoxides (20–40% on the rate of absorption of oxygen at 130°C), the shortness of surviving hydroperoxide blocks, the formation of degradation products of low molecular weight even in the initial stages, and the proportionality of the rate of formation of such products to the concentration not of hydroperoxide but of free radicals—support [31] the latter mechanism (chain propagation by the breakdown of a considerable proportion of hydroperoxy-groups immediately after their formation). Furthermore [33] the rate constants for reaction of these radicals with a hydroperoxide are considerably larger than those for their interaction with P–H. Thus the free valency is located beside the newly formed hydroperoxy-group after abstraction of a hydrogen atom by a $PO_2^{\cdot}$ radical from a neighbouring unit of the macromolecule§; it may attack a hydroperoxy-group or the next unit of its own or a neighbouring macromolecule, or add oxygen to form a new $PO_2^{\cdot}$ radical [35–36]:



(8)

(9)

(10)

The first process leads to destruction of the hydroperoxide just formed, whereas the latter two processes remove the reaction centre and stabilise this group, to give a yield of stabilised hydroperoxide of [35]

$$\alpha = \frac{k'' + k'''[O_2]}{k' + k'' + k'''[O_2]},$$

$$\frac{1}{\alpha} = 1 + \frac{k'}{k'''([O_2] + k''/k''')}.$$

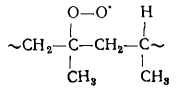
These equations show that α should depend on the oxygen pressure. The latter formula permits determination of the ratio k''/k''' of the rates of the second and third processes.

As a result of this first process hydroxyl and carboxyl groups appear within the hydroperoxide block, in both α- and β-positions with respect to tertiary and secondary hydroperoxy-groups. This process leads to rupture of the chain. The second process disturbs the regular arrangement of hydroperoxy-groups. Since the ratio of the sum of the rates of (8) and (9) to the rates of reaction (10) will depend on the concentration of molecular oxygen in the polymer, the composition of the block and the properties of the polymer hydroperoxides will depend on the oxygen pressure. Taking into account all three processes involving the $PO_2^{\cdot}$ radical, we are able to explain many experimental aspects of the oxidation of polyalkenes [31–35].

‡ The role of such reactions was shown earlier [14,15] in the co-oxidation of simpler organic compounds.

§ The $PO_2^{\cdot}$ macroradicals formed by oxidation of a polymer react mainly with a neighbouring unit in their own macromolecule [32,34].

Products of low molecular weight can be formed also by the direct decompositon of a single radical



Competition between two reactions of chain propagation—the unimolecular isomerisation and breakdown of peroxy-radicals (to form many different products with rupture of the initial carbon skeleton)

$$RO_2^{\cdot} \rightarrow R'HO + R''O^{\cdot},$$

and the bimolecular reaction

$$RO_2^{\cdot} + RH \rightarrow ROOH + R^{\cdot}$$

with formation of a hydroperoxide as sole primary product—governs the composition of the oxidation products of simple organic compounds [10,11,37]. Since the corresponding activation energies are ~20 and ~10 kcal mole^{-1}, the proportion of unimolecular reactions (yielding simple degradation products) will increase with rise in temperature, and the contribution of unimolecular reactions to the oxidation of compounds of low molecular weight is usually negligible below 100°C. However, the relative proportions of the two reaction paths is determined not only by the temperature but also by the frequency of the collisions necessary for a bimolecular process. This may be responsible for the significantly larger contribution to the solid-phase oxidation of polymers made by unimolecular reactions leading to the formation of simple reaction products.

The above conditions mark the limits within which the step-by-step mechanism of migration of the free valency plays a decisive part in the oxidation of polymers. The role of this mechanism should diminish as low-molecular products accumulate, and the free valency will migrate mainly by means of reaction products possessing sufficient mobility in the polymer matrix [38]. Denoting by rH the low-molecular-degradation products, we can represent displacement of the free valency as

$$P^{\cdot} + rH \xrightarrow{k_2''} PH + r^{\cdot}.$$

The resulting low-molecular radical r$^{\cdot}$ (alkyl or, in the presence of molecular oxygen, peroxy) moves a distance

$$\lambda = \sqrt{6D_0\tau}$$

during its lifetime τ. At temperatures above 100°C the diffusion coefficient D_0 for rH and r$^{\cdot}$ lies in the range 10^{-6}–10^{-8} cm^2 s^{-1}, so that λ may reach several micrometres [38–40]. Destruction of the radical r$^{\cdot}$ by the reaction

$$r^{\cdot} + PH \xrightarrow{k_3''} rH + P \qquad (11)$$

is equivalent to the macroradical P$^{\cdot}$ "jumping" a distance $\lambda = (6D_0\tau)^{1/2}$, the frequency of such jumps being $\nu = k_2''[rH]$. [34] The coefficient for chemical diffusion of the radical P$^{\cdot}$ is

$$D_1 = D_0 k_2''[rH]\tau.$$

On the assumption that r$^{\cdot}$ is removed solely by reaction (11), we obtain $\tau = 1/k_3''[PH]$, and then $D_1 = D_0 k_2''[rH]/k_3''[PH]$. Provided that $D_0 \simeq 10^{-7}$ cm^2 s^{-1}, $[rH] \simeq 6 \times 10^{-6}$ mole cm^{-3}, and $k_2''/k_3'' \simeq 1$–100¶ we have $D_1 \simeq 10^{-8}$–10^{-10} cm^2 s^{-1}. Such a rate of migration of the free valency ensures propagation of the oxidation chain in the solid polymer, since in many cases [38] the rate provided by the step-by-step mechanism is far lower.

The recombination of radicals may also be due to the involvement of low-molecular degradation products [38–41]:

$$\left.\begin{array}{l} r^{\cdot} + P^{\cdot} \xrightarrow{k_4'} \\ r^{\cdot} + r^{\cdot} \xrightarrow{k_5'} \end{array}\right| \longrightarrow \text{Stable products.}$$

Provided that $k_4' \simeq k_5'$, we have

$$-\frac{d[P^{\cdot}]}{dt} = 2k_4' \frac{k_2''[rH]}{k_3''[PH] + k_4'[P^{\cdot}]}[P]^2.$$

When $k_4'[P^{\cdot}] \ll k_3''[PH]$, we find that

$$-\frac{d[P^{\cdot}]}{dt} = 8\pi d_1 D_0 \frac{k_2''[rH]}{k_3''[PH]}[P^{\cdot}]^2,$$

where d_1 is the sum of the radii of the colliding particles. Substituting the values $d_1 \simeq 5 \times 10^{-8}$ cm, $D_0 \simeq 10^{-7}$ cm^2 s^{-1}, $k_2''/k_3'' \simeq 200$, $[rH] = 5 \times 10^{-6}$ and $[PH] = 0.025$ mole cm^{-3}, we obtain a chain-termination rate constant of 3.5×10^9 cm^3 mole^{-1} s^{-1} (the corresponding experimental values is 9×10^9).

Another important feature of a crystalline polymer is a complicated supermolecular structure comprising alternating regions differing in degree of ordering of the polymer chain. In general we must regard a polymer specimen as consisting of various microregions of varying reactivity. The relative arrangement and dimensions of such regions, as well as the specific volumes of the various structural components, depend on many factors. The stability of a polymer is considerably influenced by the degree of ordering of the polymer chains in the solid [19,31,42–44].

The rate of interaction of a gas A with a polymer comprises the reaction velocities in the individual structural components:

$$W_a = \sum_j \rho_j W_{aj},$$

where ρ_j is the specific volume of the jth structural component and W_{aj} the rate of reaction in this component. For a second-order reaction

$$W_{aj} = k_{aj}c_j[A]_j = k_{aj}c_j\gamma_{aj}^{-1}p_a,$$

where k_{aj} is the rate constant, c_j the polymer concentration, γ_{aj} the solubility coefficient of A (all for the jth component), and $p_a = \gamma_{aj}[A]_j$ is the partial pressure of A outside the polymer. When a chain reaction occurs in an individual structural unit, the process is complicated by the migration of active centres through the boundary of this unit. Oxidation does not usually involve the crystalline regions of a polymer [43]: the solubility of oxygen is low in regions having an undistorted crystal lattice [16,18], while the reactivity of the macromolecules is diminished in these segments, since the lattice prevents formation of the optimum configuration of the activated complex [45].

It has been shown for the oxidation of polypropylene that finely spherulitic specimens are oxidised more rapidly than coarsely spherulitic specimens at different stages of the process. In the former case the reaction is probably localised mainly in the interspherulitic material. In a coarsely spherulitic polymer, where the proportion of such material is insignificant, the process occurs predominantly in the interfibre portions within the spherulite. During extensive oxidation, when radicals decay mainly by

¶ The reality of these postulates was validated in Ref. 38.

quadratic termination†, the escape of radicals from amorphous layers into the crystalline material plays a subordinate role, and the rates of oxidation of specimens having the same "crystallinity" differ insignificantly.

The observed difference between rates of oxidation of specimens differing in supermolecular structure is more strongly marked the lower the reaction temperature, and it disappears at the melting point. The presence of inhomogeneities in a polymer, as well as differences in the solubility of an inhibitor in regions of the polymer differing in degree of organisation[16-19], demands a special study of non-uniformly inhibited polymers[46-50]. Such cases are indeed found, since a non-uniform distribution of an inhibitor may result from technical defects in the preparation of the specimen.

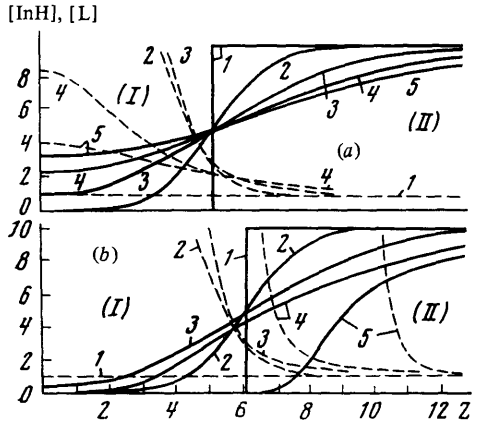


Figure 3. Distribution of relative concentrations of inhibitor [InH] (full curves) and of active centres [L] (broken curves) along a unidimensional specimen of length Z with section (I) initially uninhibited ([InH] = 0) and section (II) initially inhibited ($[InH]^{I,0}_{II,0} = 10$) for: *a*) smaller section (I); *b*) larger section (I) after different times of oxidation τ (in relative units): 1) 0; 2) 1; 3) 5; 4) 10 (12.5 in case *b*); 5) 15 (17.5).

If the inhibitor is initially absent from some part of the specimen, and neither inhibitor nor active degradation centres are able to diffuse, an autocatalytic reaction should occur in this portion independent of its size. But diffusion of inhibitor into the uninhibited region (and of active centres outwards) may result either in decay of the reaction or of gradual extension of the autocatalytic reaction throughout the specimen. Hence diffusion of inhibitor and of active centres must in general be considered when the initial distribution of inhibitor in the oxidisable specimen is non-uniform. Fig. 3 illustrates the theoretically calculated concentration distributions of inhibitor and of active centre [InH] and [L] along a unidimensional specimen after various time intervals. In both cases (*a*) and (*b*) both inhibitor and active-centre concentrations increase initially on the originally uninhibited segment. However, a difference then develops: if the size of the uninhibited portion Z is smaller than a limiting value Z_{cr}, the reaction dies out; if $Z > Z_{cr}$, a front is formed, and the reaction extends throughout the specimen. The critical value Z_{cr} depends on the concentration of inhibitor in the specimen $[InH]_{II,0}$ and on the ratio of the diffusion coefficients of inhibitor and of active centre. Both cases have been achieved in practice (Fig. 4)[47,48]. Fig. 5 shows the dependence of the induction period in the oxidation of polypropylene on the concentration of a diamine either uniformly or non-uniformly distributed in the polymer. The inflexion on curve *1* corresponds to the critical inhibitor concentration required to halt the process[50]. The inflexion on curve *2*, representing non-uniform inhibition, corresponds to the concentration at which the critical size of the uninhibited part of the polymer becomes equal to the actual size of the largest of the central segments of the powder particles devoid of inhibitor.

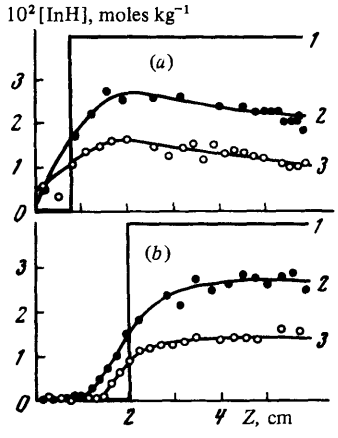


Figure 4. Distribution of actual concentrations of methylenebis-2-(4-methyl-6-t-butylphenol) [InH] in atactic polypropylene (size of specimen Z), with initially uninhibited portions of: *a*) 0.8 cm; *b*) 2 cm and initial inhibitor concentration in inhibited portion $[InH]_{II,0} = 0.04$ mole kg^{-1}, after oxidation in air at 190°C for different periods (min): 1) 0; 2) 150; 3) 300.

The investigation of oxidation processes in polymers at low temperatures is of great interest for the storage and performance of articles. Polymers are processed at high temperatures (as melts), under which conditions the specific features of low-temperature solid-phase oxidation[12,30-32,51] disappear, and new problems connected with the mechanism of high-temperature oxidation appear[51-53]. In spite of the precautions adopted in technology (e.g. processing in an atmosphere of an inert gas) the properties of the polymer change during processing, since degradation or cross-linking of the polymer chains takes place.

† In the early stages (at a low rate of initiation of radicals), when the concentration of radicals is small, decay occurs linearly, by migration of the free valency into the crystalline phase. In a finely spherulitic polymer the crystallites are too small for the radicals that have entered them to be able to react with oxygen.

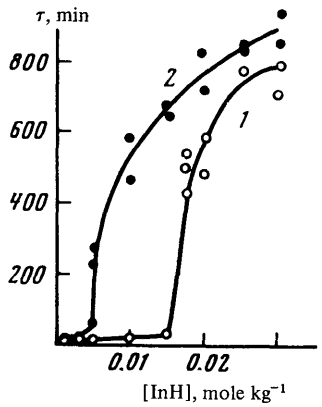


Figure 5. Dependence of induction period τ on concentration of dimethylbis-*p*-phenylaminophenoxysilane (S-1) [InH] in the oxidation of isotactic polypropylene of particle size 0.03 mm in oxygen (300 mmHg) at 200°C: 1) inhibitor applied to surface of pellets to give a non-uniform distribution; 2) pellets then heated in a vacuum at 100°C to give a uniform distribution of inhibitor.

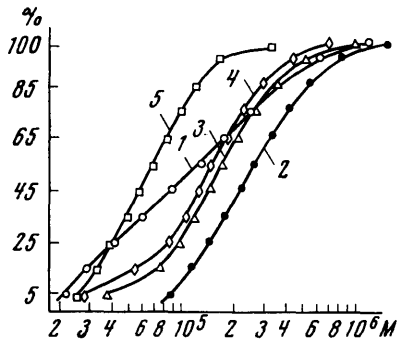


Figure 6. Dependence of molecular mass M distribution function on number of processings: 1) initial medium-pressure polyethylene; 2) polymer after first processing; 3) after second processing; 4) after third processing; 5) after thermal oxidation.

One of the most sensitive methods for recording the degradation and the cross-linking of macromolecules is analysis of the molecular-mass distribution function MMD.[29,53-56] For example, significant changes in molecular weight during multiple extrusions of (action of high temperatures and shear stresses on) high-density medium-pressure polyethylene are revealed[29] by analysis of the MMD function (Fig. 6). After the first processing the distribution curve of the initial polymer, which possesses a comparatively wide distribution (curve *1*), contracts and shifts to higher molecular weights (curve *2*). Subsequent processings produce the reverse process (curves *3* and *4*): they result in degradative processes leading to a decrease in molecular weight. In the absence of mechanical action on the polymer (subjected only to thermal oxidation) the latter undergoes only degradation (curve *5*). Degradation is probably[29] associated with thermal oxidation, whereas mechanical action is responsible for cross-linking.

Another effective method for studying ageing processes is use of a paramagnetic probe[57-67]. It consists essentially in measuring the electron spin resonance spectra of stable radicals introduced into the polymer, and calculating the appropriate parameters. The form of e.s.r. spectrum indicates structural features of the polymer matrix[57]. The following points must be borne in mind when the method is used[57].

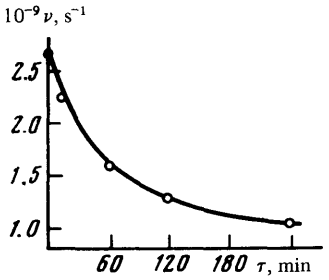


Figure 7. Dependence of rotational frequency ν of probe radical on time of oxidation of polypropylene in oxygen (400 mmHg) at 130°C.

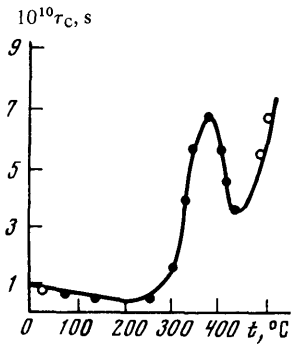


Figure 8. Dependence of correlation time of probe $\tau_c = \nu^{-1}$ on limiting temperature of initial heating of methylvinylsiloxane rubber.

Firstly, the rotational and translational mobility of stable radicals introduced into polymers indicates the intensity of molecular movements of the polymer matrix. Degradation is accompanied by a change in the molecular mobility of segments of the polymer chains, which is apparent in a change in the frequency of rotation of the probe radical. For example, a decrease in frequency during thermo-oxidative degradation (Fig. 7) corresponds to decreases in movements of segments in the amorphous phase of the polymer. In this case cross-linking occurs during oxidation. A more complicated case is illustrated by Fig. 8, where the ratio of the contributions of degradation and cross-linking changes several times with rise in temperature.

Secondly, stable radicals simulate the behaviour of simple compounds in a polymer (initiators, inhibitors, etc.), their rotational and translational mobility, and their local sites and local concentrations, which is important for calculating elementary constants for the reactions of macromolecules with simple substances.

Information obtained from study of the kinetics and the mechanism of the thermo-oxidative degradation of polymers is used [21-23] in selecting the most effective antioxidants, among which derivatives of phenols and amines are of considerable interest, as before. Among the attributes which the most efficient stabilisers should possess are (i) high rate constants of reaction with radicals (primarily peroxy and alkyl [10])

$$InH + PO_2^{\cdot}(P) \rightarrow POOH(PH) + In^{\cdot} \qquad (12)$$

(ii) a relatively inactive radical In$^{\cdot}$ formed by the action of P$^{\cdot}$ or $PO_2^{\cdot}$ on InH, [10] (iii) reaction products that are preferably effective stabilisers [21-23], and (iv) more than one functional group in the molecule [21-23,68]. Highly efficient new antioxidants have recently been prepared [for polyalkenes, polyoxymethylene, polystyrene, polychlorides, synthetic rubbers, cellulose ethers, poly(vinyl chloride), and other polymers]—the S series of stabilisers [69-72] (stabiliser S-1 is dimethylbis-*p*-phenylaminophenoxysilane).

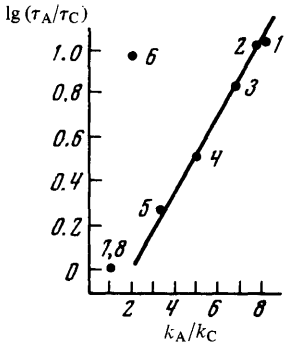


Figure 9. Dependence of $\lg(\tau_A/\tau_C)$ on k_A/k_C for: 1) *NN'*-dioctyl-*p*-phenylenediamine; 2) *NN'*-di-isopentyl-*p*-phenylenediamine; 3) *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine; 4) *NN'*-bis-α-methylbenzyl-*p*-phenylenediamine; 5) *N*-α-methylbenzylanisidine; 6) *NN'*-dibutylthiourea; 7) thiobis-2-(4-methyl-6-t-butylphenol); 8) methyl oleate.

Another important problem is to protect polymers from the action of ozone. Kinetic investigations [73] have established correlations between the rate of reaction of ozone with the test antiozonant under model conditions and the efficiency of the latter in rubbers (Fig. 9):

$$\lg\frac{\tau_A}{\tau_c} = N + M\frac{k_A}{k_c},$$

where N and M are constants, τ_A and τ_C are the induction periods for ozonisation of rubber containing the antiozonant A and of a control compound (model alkene) respectively, and k_A and k_C are the rate constants for reaction of ozone with A and with the control. The above relation not only simplifies and accelerates the testing of new potential ozonants (since little time is required to measure the rate constants for reaction with ozone) but also guides the preparation of new antiozonants.

The efficiency of the usual stabilisers (amines, phenols, and phosphorus-containing and sulphur-containing compounds) in polymers decreases with rise in temperature independently of their mechanism of action; at 270–300°C they become completely ineffective [74,75]. The reasons are that at high temperatures the In$^{\cdot}$ radicals formed by reactions (4) and (5) become reactive and capable of propagating chains, the inhibitor itself is readily oxidised, and the In–H bond is weak, so that the inhibitor becomes an initiator yielding free radicals.

Finely divided metals (M), generated by decomposition of their organic salts (e.g. oxalates) in polymer compositions during the service life of articles, are effective stabilisers against thermo-oxidative degradation at temperatures above 300°C. [76-79] The rate at which such metals react with oxygen exceeds considerably the rate at which oxygen reacts with the polymer and with the radicals formed by the degradation of polymers:

$$W_{M+O_2} \gg W_{PH+O_2}, W_{P^{\cdot}+O_2}.$$

Thus oxygen plays almost no part in chain initiation and propagation, but is entirely absorbed by reaction with the metal.

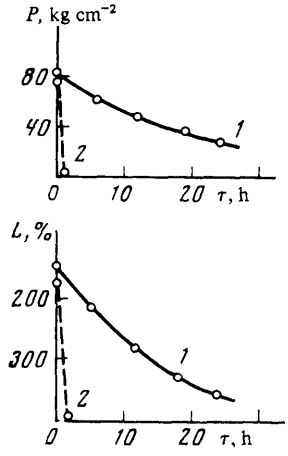


Figure 10. Variation in strength P and relative elongation L at rupture of SKTV-2 silicone rubber during ageing in air at 350°C: 1) specimen stabilised with finely divided copper; 2) control specimen stabilised with iron sesquioxide.

The lifetime of a polymer τ_p depends on the thickness of the specimen l and the solubility of oxygen in the polymer σ_x:

$$\tau_p = K\frac{l^2[M]}{D\sigma_x},$$

where K is a constant determined by the stoichiometry of the process and D is the diffusion coefficient of molecular oxygen. Figs. 10 and 11 show that specimens stabilised by finely divided metals retain their properties several

times longer. This method of stabilisation is suitable not only for polyorganosiloxanes but in principle for all polymers for which the relation $W_{M + O_2} > W_{PH + O_2}$ is satisfied (Fig. 12) under the working conditions of articles made from them.

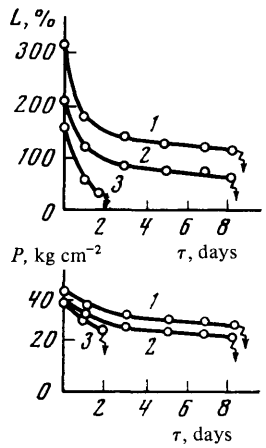


Figure 11. Variation in strength P and relative elongation L at break of siloxane rubber during ageing in air at 350°C: 1) specimen stabilised with finely divided copper; 2) specimen stabilised with finely divided iron; 3) standard specimen stabilised with titanium dioxide. The arrows show the beginning of rapid breakdown of the polymer; those on curves *1* and *2* correspond to exhaustion of the stabiliser.

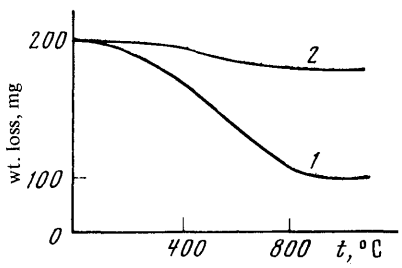


Figure 12. Thermogravimetric curves for a carbonised fibre: 1) unstabilised specimen; 2) specimen stabilised with finely divided copper.

IV. PHOTO-OXIDATIVE DEGRADATION

The photo-oxidation of a polymer comprises a complicated set of physical and chemical processes occurring under the influence of light [80-97]. It is extremely important to be able to calculate the absolute rate of photo-oxidation of a solid polymer, since this will enable the life of articles to be predicted. This was first accomplished for the photo-oxidation of polypropylene [80-82], where analysis of all possible reactions revealed a chain reaction with degenerate branching at hydroperoxides and with quadratic chain termination. Oxidation can be represented by the scheme

$$X \xrightarrow{h\nu} PO_2^{\cdot};$$

$$POOH + h\nu \xrightarrow{\varphi} PO^{\cdot} + {}^{\cdot}OH \xrightarrow{2O_2 + 2PH} 2PO_2^{\cdot} + H_2O + K;$$

$$K + h\nu \xrightarrow{2O_2} PO_2^{\cdot};$$

$$PO_2^{\cdot} + PH \xrightarrow[O_2]{k_2} POOH + PO_2^{\cdot};$$

$$PO_2^{\cdot} + PO_2^{\cdot} \xrightarrow{k_4} K + POH + O_2;$$

where **X** represents impurities in a polymer **PH** and **K** is a ketone, while φ is the quantum efficiency of the photochemical reaction. This scheme yields for the concentration of carbonyl compounds formed during photo-oxidation the formula

$$\frac{[K]}{[POOH]_\infty} = \alpha t - 2\left(3 - e^{-\frac{\alpha t}{4}}\right)\left(1 - e^{-\frac{\alpha t}{4}}\right),$$

where

$$\alpha = \int I \varepsilon d\lambda, \quad [POOH]_\infty = \frac{4k_2^2[PH]^2}{\alpha k_6}.$$

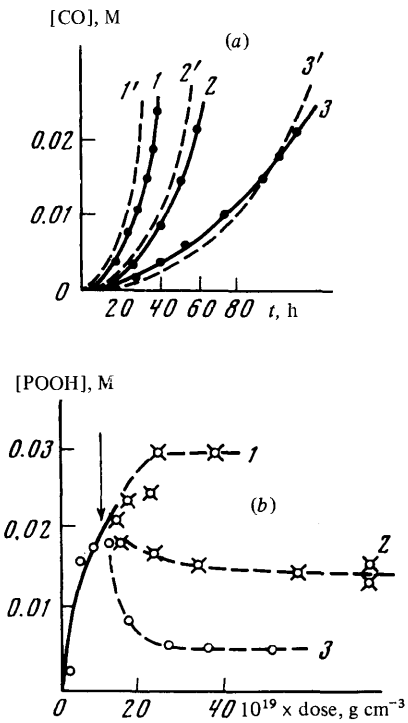


Figure 13. Comparison of experimental results (curves with points) with calculated values (broken curves, primed) for the photo-oxidation of polyalkenes. (*a*) Kinetic curves for the accumulation of carbonyl compounds under the influence of light of different wavelengths (nm): 1,1′) 280; 2,2′) 295; 3,3′) 305. (*b*) Kinetic curves for the accumulation of hydroperoxides during the photo-oxidation of polypropylene containing Methylox antioxidant (0.1 mole kg^{-1}), where the relative light intensity was changed at the time indicated by the arrow from 4 to: 1) 0.7; 2) 1.4; 3) 4 (by this time the Methylox was exhausted).

The data used in the calculation‡ included the intensity I, the absorption coefficient ϵ and the spectral distribution of the light source, and the absorption spectrum and the quantum efficiency of photodecomposition of the hydroperoxide; values of $k_2/k_6^{1/2}$ were taken from work on the dark initiated oxidation of the polymer. Fig. 13 shows good agreement between calculation and experiment, which confirms the reliability of the suggested scheme. Such agreement opens up the possibility of using polypropylene as a model polymer in investigating the mechanism of the action of photostabilisers.

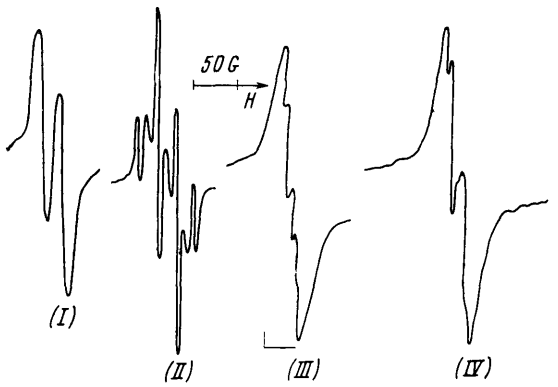
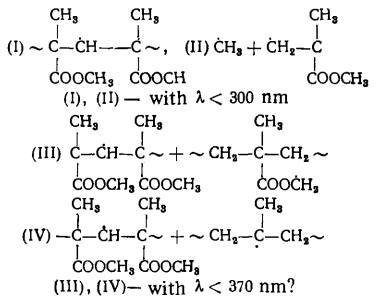
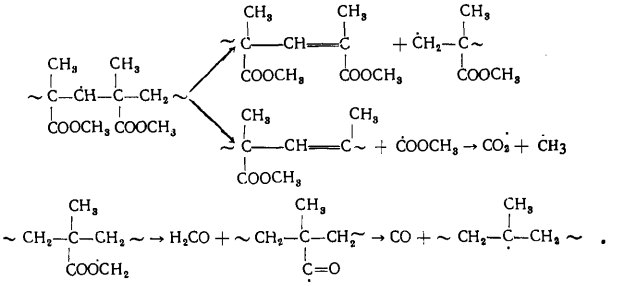


Figure 14. Electron spin resonance spectra of certain radicals obtained in the photo-oxidation of poly(methyl methacrylate):



The action of light on a polymer usually gives rise at once to several chemical processes occurring at different rates. To determine the contributions made by each of these reactions it is extremely important to know the quantum efficiencies of the remaining processes [83-85,90-92]. With poly(methyl methacrylate), whose ester groups are responsible for absorption, the principal photochemical process was the rupture of ester groups with a quantum efficiency close to unity [88,91,92]; this was accompanied by the transformation of methylene groups, chain cleavage, and the accumulation of radicals in order of diminishing quantum efficiency (respectively ~0.1, 0.012, and 0.001). Many details of the mechanism of the photo-oxidation of this polymer have been elucidated from the quantum efficiencies together with the application of ultraviolet, infrared, and e.s.r. spectroscopy to its kinetic investigation [91-93]. Fig. 14 illustrates the e.s.r. spectra of intermediate free radicals recorded in the polymer, in which the main photochemical reactions are



Photoconversion in cellulose triacetate is also due to the absorption of light by ester groups. The breakdown of such groups and of ether groups and the accumulation of carbonyl compounds, hydroxy-groups, and acetic acid have respectively quantum efficiencies of 0.015, 0.01, 0.005, 0.005, and 0.005.

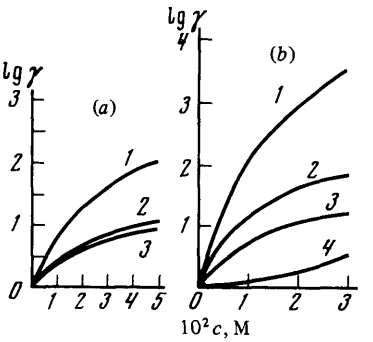
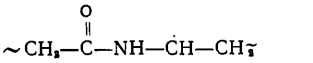


Figure 15. Coefficient of inhibition of the oxidation of diphenylmethane γ photosensitised by benzophenone (λ = 365 nm) as a function of the concentration of the photostabiliser: *a*) 2-hydroxy-4-octyloxybenzophenone; *b*) 2-(2-hydroxy-5-methylphenyl)benzotriazole: 1) total effect; and contributions made by: 2) shielding; 3) quenching; 4) inhibition.

The absorption of light by polyhexanamide is most effective in causing the absorption of oxygen (φ = 0.06); [90] rupture of the chain and evolution of carbon monoxide have φ = 0.015; and the quantum efficiencies of the accumulation of carbonyl and carboxyl groups are respectively 0.009 and 0.005. Under the influence of light

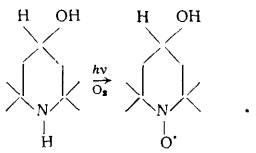


radicals decompose with the formation of ~$[CH_2]_5-\dot{C}=O$ radicals, which are then converted into ~$CH_2-\dot{C}H_2$ and ~$CH_2-\dot{C}H-CH_2$~ radicals [94].

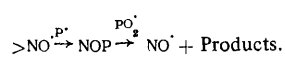
‡ The calculations were based on the usual equations of homogeneous chemical kinetics, since the photo-oxidation of polypropylene was investigated at temperatures above the glass point T_{gl}. However, processes occurring in a polymer below this temperature exhibit kinetic peculiarities—inhibition of chemical conversion during the process and kinetic arrest of the reaction [80].

Photostabilisers act by three main mechanisms: they absorb photochemically active light, quench excited states, and inhibit dark oxidation [88]. For two typical ultraviolet absorbers Fig. 15 shows the concentration dependence of the total reaction inhibition coefficient and the contributions made by shielding, quenching, and inhibition. Since the quantum efficiency is approximately unity for poly(methyl methacrylate), the photoreaction is so rapid that deactivation cannot occur, and therefore the efficiency of photostabilisers is here determined solely by their ability to absorb light. In cellulose triacetate, ester groups are decomposed with a quantum efficiency of 0.015, deactivation processes are competitive, and the photostabilisers that protect poly(methyl methacrylate) by a shielding mechanism act in cellulose triacetate by a quenching mechanism.

In the photo-oxidation of several polymers (e.g. polyhexanamide [88,90]) in the kinetic range in air, only a proportion of alkyl radicals are converted into peroxy-radicals. Thus such polymers can be stabilised by inhibitors that react with both types of radicals. Considerable inhibition is observed in the presence of stable nitroxyl radicals, which react only with alkyl radicals, and of chelate complexes of metals of variable valency, whose activity increases as the partial pressure of oxygen falls. In this connection great interest attaches to highly efficient new photostabilisers—secondary and tertiary aliphatic amines, derivatives of piperidine [22,87-102]—possessing neither shielding nor inhibiting effects and exerting only a weak quenching action. These compounds function [87] by photosensitised conversion of the amines into nitroxyl radicals, which are known to act as photostabilisers:

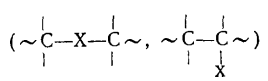


Prolonged inhibition is observed in the presence of such compounds (the stoichiometric coefficient may [63] exceed 10). The nitroxyl radical is regenerated from its reaction product with the alkyl radical by the action of a peroxy-radical:



V. HYDROLYTIC DEGRADATION

Polymers containing heteroatoms X in main and side chains



are hydrolytically unstable§. Hydrolytic degradation of a polymer involves diffusion of the active medium into the polymer and reactions involving chemically unstable bonds [103,104]. Several investigations are being undertaken in conformity with this—(i) use of simple model compounds to study the mechanisms of the conversion of hydrolytically unstable bonds of polymers in active media, (ii) determination of the main types of breakdown undergone by molecules of various polymers, (iii) establishment of the laws of the diffusion of active media into polymeric materials, and (iv) investigation of the mechanisms of the degradation of polymeric material in active media.

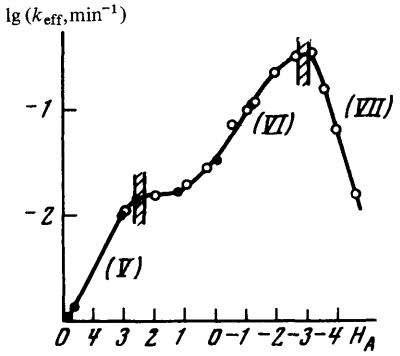
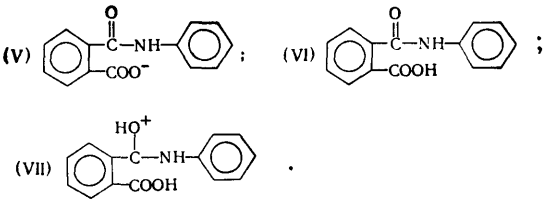


Figure 16. Dependence of effective hydrolysis rate constant k_{eff} of phthalanilic acid (at 25°C) on the acidity function H_A. The forms of the acid predominating on the various sections of the curve are



Quite detailed studies have now been made of the breakdown in acid and alkaline media of amide and imide [105-118], ether and ester [119-124], acetal [125-128], glycosidic [129-135], and siloxane [136,137] bonds. Fig. 16 illustrates the variation of $\lg k_{eff}$ with the acidity function H_A for the hydrolysis of phthalanilic acid as a model of non-cyclised units in polymers. The complexity of the dependence is explained by a mechanism in which unreactive forms are produced by protonation of the carbonyl oxygen of the amide bonds and by dissociation of the carboxy-group. The unionised form is reactive, able to react either with a carboxy-group (intramolecular catalysis along the segment H_A = 4–1) or with an oxonium ion (specific acid catalysis in more acidic solutions)¶.

Mechanisms of the hydrolytic degradation of various bonds have been surveyed [103,104]. Two types of decomposition—random and depolymerisation—can occur in polymer molecules. In the first type all hydrolytically unstable bonds are equally reactive, so that there should be no difference between a polymer and its simple analogue. In depolymerisation the effective rate constant depends on the molecular weight. In practice the two types of decomposition generally occur together [125-128].

Thus the hydrolytic degradation of polymers under homogeneous conditions can be characterised by a few true rate constants depending on the type and character of the decomposition [103,104]. In order to establish the mechanism of the degradation of polymeric materials in active media,

§ Polymers containing fluorine constitute an exception.

¶ A result of practical importance is the enhancement of the stability of amides in concentrated acids.

however, we must know how the medium diffuses in the polymer and the degree of dissociation of the electrolyte into ions [138-151]. In polymers that dissolve readily in water, e.g. poly(vinyl alcohol) (solubility 80% by mass), acids migrate with diffusion coefficients closely similar to those in aqueous solutions [144-147]. Selective sorption of electrolyte and water is observed in moderately soluble polymers, e.g. ethylcellulose (solubility 2% by mass). Fig. 17 shows the variation in the concentrations of water and hydrogen chloride during the diffusion of the vapour from 28% hydrochloric acid in ethylcellulose films at 45°C. The active medium diffuses on a single front, but the concentration ratio of water and hydrogen chloride in the polymer is approximately ten times the ratio for the gaseous phase [150].

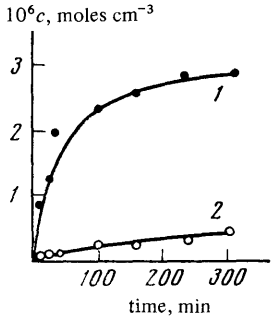


Figure 17. Variation in concentration during the diffusion of the vapour of 28% hydrochloric acid into an ethylcellulose film at 45°C: 1) H_2O; 2) HCl.

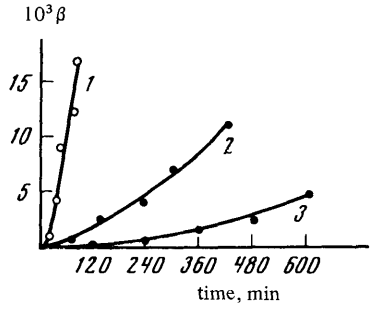


Figure 18. Time variation of degree of conversion β of ester bonds during degradation, in 53% sulphuric acid at 116°C, of poly(ethylene terephthalate) films varying in thickness (μm): 1) 5 ± 1; 2) 20 ± 2; 3) 80 ± 5.

Water and sulphuric acid diffuse at significantly different rates in sparingly water-soluble polymers, e.g. poly(ethylene terephthalate): the diffusion coefficient of water exceeds that of sulphuric acid by a factor of 10^5. [118,124] In the chemical degradation of polymers the rate of diffusion of the active medium is frequently comparable with the rate of the chemical reaction, and degradation takes place within a reaction zone whose size increases with time, ultimately reaching the size of the article. Fig. 18 illustrates the time dependence of the degree of conversion of ester bonds during the degradation of poly(ethylene terephthalate) films in 53% sulphuric acid at 116°C. [118,120,121] With a thin film (5 μm) the rate is constant after 30 min, since the acid has saturated the polymer. With films 20 and 80 μm thick the rate increases with time, as the quantity of acid in the films increases. The equations obtained kinetically permit quantitative prediction of the chemical stability of poly(ethylene terephthalate) over wide ranges of acid concentration, temperature, and time [118,120,121].

A correct interpretation of kinetic data for structurally non-uniform polymer materials requires information on the accessibility of functional groups. Hydrogen–deuterium exchange provides a convenient method for determining such accessibility in polymers having mobile hydrogen atoms [138-143]. The accessibility of amide bonds in polyhexanamide, for example, is a function of temperature (Fig. 19): at 150°C all such bonds, including those in crystalline regions, are accessible to hydrogen–deuterium exchange.

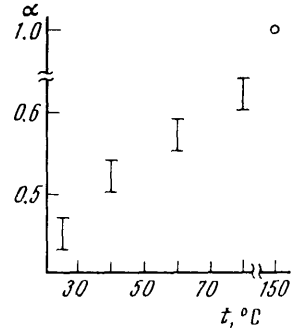


Figure 19. Temperature dependence of accessibility α of amide bonds in polyhexanamide films.

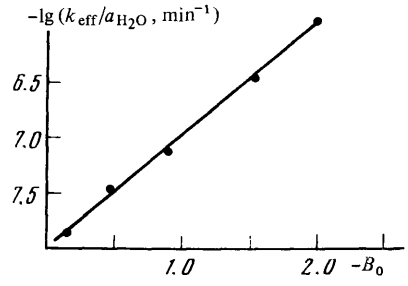


Figure 20. Dependence of $\lg(k_{eff}/a_{H_2O})$ on alkalinity function B_0 of aqueous potassium hydroxide for the degradation of poly(ethylene terephthalate) films 68 ± 2 μm thick.

In concentrated solutions the rate of chemical reaction far exceeds the rate of diffusion of molecules of the active medium into the polymer, and degradation takes place in a thin surface layer. An example is the breakdown of poly(ethylene terephthalate) film in aqueous alkalis [118,122,123].

The reaction is zero order with respect to the polymer, and the absence from the infrared multiple diffuse total internal reflection spectra of absorption bands due to decomposition products suggests that the depth of reaction approximates to a monolayer. Degradation of this type is characterised by two laws: (i) the effective rate constant is simply related to the thermodynamic parameters—the activity of water and the alkalinity function—of the aggressive medium (Fig. 20); and (ii) degree of crystallinity and orientation have hardly any effect on the kinetic parameters.

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The results discussed above, obtained from kinetic studies of various types of polymer degradation (thermal, thermo-oxidative, photo-oxidative, and hydrolytic), apply to polymers in an unstressed state. This covers by no means all the degradation processes encountered in practice. Development of a theory of the degradation of polymeric materials in a stressed state is an urgent task of the science of polymer degradation.

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Testing of Chemical Compounds as Stabilisers for Polymeric Materials

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Test methods are briefly surveyed, a scheme of testing is examined, and experimental results obtained by means of the scheme are discussed. A list of 69 references is included.

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I. INTRODUCTION

Most cases of the degradation of polymeric materials involve a free-radical chain mechanism; this enables the rate of degradation to be lowered substantially by introducing into the polymer a small quantity of a special substance to act as a stabiliser. The latter often functions either by deactivating the active radicals in the chain process or by decomposing intermediate products that provide a source of active radicals. In view of the continuous growth in the manufacture of various polymeric materials and substances for their stabilisation, the testing of chemical compounds as stabilisers has become an urgent problem.

On the basis of achievements of current research on the kinetics and the mechanism of chain processes a team including the Reviewers, headed by Academician N. M. Emanuel'[1-3] at the Institute of Chemical Physics of the USSR Academy of Sciences, has developed during recent years a set of methods for the rapid and reliable quantitative assessment of various chemical compounds as potential stabilisers for polymers whose degradation takes place by a free-radical chain mechanism. The scheme includes methods for preliminary assessment of effectiveness on model reactions (screening) and methods for the accelerated testing of compounds in polymers and polymeric materials.

II. PRELIMINARY ASSESSMENT BY MEANS OF MODEL REACTIONS

The testing of a chemical compound begins with a quantitative assessment of its chemical reactivity on model systems. Thus oxidative degradation is simulated by chain oxidation of simple compounds, whose mechanism has now been studied quite thoroughly[4-8]. The applicability of such reactions as models has a theoretical basis in the common mechanism of oxidation of organic compounds having low and high molecular weights[9-11]. In particular, peroxy-radicals function as active centres in these chain processes. The active centres in the thermal degradation of polymers are often alkyl radicals. Chain polymerisations, whose mechanism has also been thoroughly studied[12-19], are therefore used as models of thermal degradation.

The effectiveness of a chemical compound as a potential stabiliser is determined by its ability to slow down initiated chain oxidations[20,21] and polymerisations[21-23]. Various kinetic parameters, characterising such retardation, can be used as criteria of efficiency. Examples are the ratio of the rates of reaction in the absence and in the presence of the test compound, the decrease in the extent of the process (yield of polymer), etc.

Initiated oxidations and radical polymerisations can be represented by the simple scheme

(A) Chain initiation; W_i — rate of initiation , (1)

(B) Chain propagation: $R_1H + n_1 \xrightarrow{k_{p11}} n_1 +$ Product , (2)

(C) Chain termination: $2n_1 \xrightarrow{k_{t11}}$ Inactive products , (3)

where R_1H is the hydrocarbon or the monomer, n_1 is an active centre, and k_{p11} and k_{t11} are the rate constants of chain propagation and termination respectively. For sufficiently long chains the rate of the process is given by the equation

$$W = W_i^{1/2} \frac{k_{p11}}{k_{t11}^{1/2}} [R_1H]. \quad (4)$$

A more general scheme for a chain process in the presence of a substance R_2H (which may be a stabiliser) can be written

(A) Chain initiation; W_i — rate of initiation ,

(B) Chain propagation:
$R_1H + n_1 \xrightarrow{k_{p11}} n_1 +$ Product ,
$R_1H + n_2 \xrightarrow{k_{p12}} n_1 +$ Product ,
$R_2H + n_1 \xrightarrow{k_{p21}} n_2 +$ Product ,
$R_2H + n_2 \xrightarrow{k_{p22}} n_2 +$ Product ,

(C) Chain termination:
$2n_1 \xrightarrow{k_{t11}}$ (5)
$n_1 + n_2 \xrightarrow{k_{t12}}$ Inactive products . (6)
$2n_2 \xrightarrow{k_{t22}}$ (7)

The rates of the chain conversion of each substance and the overall rate of the process are described by the well known formulae for rates of co-oxidation and copolymerisation. These rates depend on the concentrations of R_1H and R_2H and the rate constants of chain propagation and termination. At low concentrations of R_2H (stabiliser

concentrations usually amount to 0.1–2%) the chain process is slowed down provided that[24]

$$\frac{k_{t12}}{k_{t11}} \cdot \frac{k_{p21}}{k_{p12}} - 2\frac{k_{p21}}{k_{p11}} > 1 .$$

Thus retardation depends on the choice of model reactions (rate constants k_{p11} and k_{t11}) and also on the three primary reactions involving R_2H and the radical formed from it. The greatest retardation is produced by substances that react rapidly with active centres (high rate constant k_{p21}) and by those from which unreactive radicals are formed (low rate constant k_{p12}).

If the additive is an inhibitor, i.e. if the radicals formed from it are inactive, we have $k_{p12} = 0$, and retardation of the chain process becomes indefinitely large. An expression for the rate of consumption of R_1H in an inhibited chain process (with $k_{p12} = 0$ and $k_{p22} = 0$) can be obtained only by making certain assumptions about the chain-terminating reactions[25]. The simplest formula is obtained by neglecting reaction (5)—quadratic termination of active centres n_1 (all active centres react with the inhibitor):

$$W_{inh} = W_i \frac{k_{p11}}{k_{p21}} \cdot \frac{(R_1H)}{(R_2H)}, \qquad (8)$$

where the inhibition coefficient $f = 1-2$ depending on the relative rates of reactions (6) and (7)†. From Eqns. (4) and (8) we find that

$$\frac{W}{W_{inh}} = \frac{f k_{p21} \cdot (R_2H)}{k_{t11}^{1/2} \cdot W_i^{1/2}} \qquad (9)$$

Thus the effect of inhibitors on the chain process is determined by the rate constant k_{p21} for reaction between inhibitor and active centre. Formula (9) can be used in many cases to assess the chemical activity of test compounds (various derivatives of amines, phenols[26], and other compounds that inhibit chain processes usually serve as stabilisers).

The rate constant k_{p21} is usually denoted by k_7 in oxidations and by k_Z in polymerisations. The nature of the oxidisable substance (the radical R·) has a slight effect on k_7.[25,27,28] A correlation may therefore be reasonably expected between this constant k_7 and the stabilising effect of the test compound. Such a correlation has indeed been established for several phenols: the more readily the peroxy-radical of tetralin abstracts the hydrogen atom from the phenol (the higher the value of k_7) the more efficient is the phenol as an antioxidant for rubber[20].

Since the reactivity of an inhibitor towards a free radical is determined by the ease of abstraction of a labile hydrogen atom, those inhibitors that are active towards alkyl radicals may be active also towards peroxy-radicals. This suggestion is supported by published results[22,23].

A most important characteristic of stabilisers against oxidative degradation is their ability to decompose hydroperoxides by a molecular mechanism. The primary product of the oxidation of an organic compound is usually a hydroperoxide, which breaks down slowly into radicals capable of initiating oxidation chains, so that oxidation proceeds autocatalytically. Decomposition of the hydroperoxide by a stabiliser prevents such autocatalysis. The efficiency of a stabiliser can conveniently be assessed on a model reaction with a simple hydroperoxide (of cumene, tetralin, etc.). A correlation was shown[22] between the half-decomposition time of cumene hydroperoxide and the induction period in the oxidation of rubbers in the presence of various antioxidants. Another important parameter is the yield of radicals per hydroperoxide molecule decomposed. Increase in the rate of breakdown should be accompanied by a decrease in this yield: otherwise the test compound will catalyse the chain degradation.

The efficiency of a chemical compound in decomposing a hydroperoxide can be assessed quantitatively by two parameters—the ratios of reaction velocities and of yields of radicals in the absence and in the presence of this compound:

$$\frac{W}{W_x} < 1; \quad \frac{e}{e_x} = \frac{W_i/W}{W_{ix}/W_x} > 1$$

where W and W_X, W_i and W_{iX}, and e and e_X are the rates of breakdown, the rates of formation of radicals, and the yields of radicals in the absence and in the presence of the test compound respectively. The rate of decomposition can be determined by measuring by iodometric titration the decrease in the concentration of hydroperoxide with time. The method of inhibitors[29] (based on the induction period) or the chemiluminescence method[25] can be used to determine the rate of formation of radicals.

The effectiveness of a stabiliser is not always determined completely by its ability to terminate chains and to decompose hydroperoxides by a molecular mechanism. Its efficiency is diminished also by reaction of an inhibitor radical with a hydroperoxide molecule

$$ROOH + \dot{In} \xrightarrow{k_{-7}} R\dot{O}_2 + InH . \qquad (10)$$

The role of this reaction will be significant if[30]

$$k_{-7} \cong \frac{2k_7k_8[InH]}{k_6[ROOH]}, \qquad (11)$$

where $k_8 = k_{t12}$ and $k_6 = k_{t11}$. In the oxidation of tetralin (at 65°C) the rate constant k_{-7} reaches 10^4 M^{-1} s^{-1} for several aromatic phenols[31]. It can be shown that Eqn. (11) is satisfied with such values of k_{-7}. The role of reaction (10) can be assessed if the model oxidation is conducted in the presence of a certain quantity of a hydroperoxide.

The relative simplicity of the procedures and the possibility of evaluating rate constants enable model reactions to be used for the rapid quantitative assessment of various classes of compounds as potential stabilisers[20-23,32]. In several cases model reactions made it possible to establish the mechanism of the action of antioxidants[28,33,34] and to elucidate the nature of synergism[33,35,36].

The above advantages of model reactions of simple compounds are accompanied by the substantial defect of not reflecting the specific character of processes occurring in macromolecular compounds. Unfortunately, the mechanism of the degradation of polymers has not yet been sufficiently studied to enable these processes to be used as models. The initiated oxidation of molten polyethylene of low molecular weight[37] and that of solid isotactic polypropylene[38] have been most thoroughly studied in this respect. Kinetic results obtained in this work can be used to assess the effectiveness of compounds as stabilisers. Radical polymerisation at high degrees of conversion can be used as macromolecular model reaction with an active centre (the radical R·) to assess the efficiency of thermostabilisers[18,39].

III. ACCELERATED TRIALS OF STABILISERS

Although model reactions and reactions in polymers have much in common, stabilisers selected on the basis of model reactions require further verification of their

† The coefficient f may vary within wider limits, e.g. with inhibitors containing several functional groups.

effectiveness in the polymers themselves or in polymeric materials. This is because the efficiency of a stabiliser in a polymer is appreciably determined by several additional physicochemical factors, the most important of which are (i) the chemical stability of the stabiliser itself (with respect to the action of heat, oxygen, certain additives, etc.), (ii) the compatibility of the stabiliser with the polymer, and (iii) the effect of the solid phase on the reactivity of the stabiliser. The best method for finally assessing the efficiency of a stabiliser is, of course, to test it in the polymer under service conditions. In many cases, however, such trials last an extremely long time (for months and even years). This period can be shortened either by raising the temperature (in the cases of thermal and oxidative degradation) or by increasing the pressure of oxygen (in the case of oxidative degradation)[20].

Since polymers and polymeric materials are complicated systems, the effectiveness of stabilisers in accelerated trials is determined by the use of general mechanical and physicochemical parameters to characterise the progress of degradation. The former include elasticity, strength, etc. Among physicochemical parameters we may note viscosity and solubility, quantity of oxygen absorbed and induction period, decrease or increase in weight, thermal effects, and change in pressure caused by the evolution of simple degradation products. Definite interrelationships should clearly exist in the variation of these parameters during degradation. In the thermo-oxidative degradation of polypropylene, for example, the rate curves for viscosity, breaking load, elongation, and oxygen absorption are of the same type[40], with the most rapid changes in these parameters occurring simultaneously.

Thus two sets of methods—preliminary assessment of effectiveness in model reactions and accelerated trials in polymers—are used to test chemical compounds as stabilisers. Both sets of methods should be quite rapid, and they should give mutually consistent results for assessing the efficiency of the stabilisers and ascertaining the mechanism of their stabilising effect.

IV. SCHEME OF TESTING

It is advisable to use the well studied polymerisation of styrene and oxidation of cumene as model reactions. The rate of initiation by azoisobutyronitrile (Aibn) is calculated by means of the formula

$$W_i = ek_d[\text{Aibn}],$$

where the rate of decomposition of the initiator

$$k_d = 1.58 \times 10^{15} \exp(-30800/RT)$$

varies slightly with the nature of the solvent[41,42]‡. The yield of radicals e is close to 1.2 for aromatic hydrocarbons[43]; its values for styrene and cumene are respectively 1.1–1.2 [44,45] and 1.1,[29] and we can adopt with sufficient accuracy $e \simeq 1.1$ for both compounds§.

‡ This value of the rate constant is identical with the average value in aromatic solvents[27].

§The yield of radicals for cumene varies[29] from 1.0 to 1.25 with rise in temperature from 40 to 80°C (the temperature range normally employed for azoisobutyronitrile as initiator), so that the average value of the yield 1.1 can be adopted for all temperatures.

The method of purification described in Ref. 46 was used for styrene, and those of Ref. 42 for cumene and azoisobutyronitrile. Cumene hydroperoxide free from inhibiting impurities can be prepared relatively simply[47]. The rates of reaction of the purified specimens should approximately satisfy Eqn. (4). The rate constants of chain propagation and termination have the values—for styrene¶

$$k_{p11} = k_p = 10^{5.7} \exp(-6000/RT)\ \text{M}^{-1}\,\text{s}^{-1};$$

$$k_t = k_0 = 10^{7.9} \exp(-2000/RT)\ \text{M}^{-1}\,\text{s}^{-1};$$

and for cumene[48]†

$$k_{p11} = k_3 = 10^{6.67 \pm 0.34} \exp[-(9800 \pm 400)/RT]\ \text{M}^{-1}\,\text{s}^{-1};$$

$$k_t = k_6 = 10^{9.2 \pm 0.3} \exp[-(6000 \pm 300)/RT]\ \text{M}^{-1}\,\text{s}^{-1};$$

The rate of polymerisation of styrene can conveniently be determined dilatometrically[18], and the rate of oxidation of cumene from the absorption of oxygen[20,49]. Previous studies[47,50] have shown that the rate of decomposition of cumene hydroperoxide (at relatively low concentrations [ROOH] < 0.1 M) into cumene and the rate of breakdown into radicals can be calculated by means of the formulae

$$W = k_d \cdot [\text{RH}][\text{ROOH}],$$

$$W_i = k_i[\text{RH}][\text{ROOH}],$$

where

$$k_d = 1.1 \times 10^8 \exp(-25400/RT)\ \text{M}^{-1}\,\text{s}^{-1},$$

$$k_i = 10^8 \exp(-26200/RT)\ \text{M}^{-1}\,\text{s}^{-1}.$$

Thus two of the four reaction velocities required to characterise the ability of a test compound to decompose the hydroperoxide can be calculated (in the absence of the test compound) from published data.

The oxidation of molten polyethylene and solid isotactic polypropylene can be used as polymeric model reactions of oxidative degradation. In molten polyethylene the cumene peroxide used as initiator decomposes into radicals over the temperature range 110–145°C with[37]

$$k_i = 10^{13.5 \pm 1.0} \exp[-(32000 \pm 2000)/RT]\ \text{s}^{-1}.$$

The rate constant determined[51] in solid polypropylene at 114°C was identical with the value[52] in solid polyethylene at this temperature. It may be postulated that the rate constants for breakdown into radicals coincide over the temperature range 114–128°C, for which it was found in polyethylene that

$$k_i = 8.5 \times 10^{15} \exp(-37500/RT)\ \text{s}^{-1}.$$

Specimens of polyethylene and polypropylene purified as in Refs. 37 and 52 had the following relations between propagation and termination rate constants—for polyethylene[37]

$$k_3/k_6^{1/2} = 10^{2.7 \pm 0.5} \exp[-(11000 \pm 1000)/RT]\ \text{M}^{-1/2}\,\text{s}^{-1/2}.$$

and for polypropylene[38]

$$k_3/k_6^{1/2} = 2.7 \times 10^6 \exp(-13500/RT)\ \text{M}^{-1/2}\,\text{s}^{-1/2}.$$

Rates of oxidation of polyethylene and polypropylene are determined from the absorption of oxygen[37,38].

The model chain reactions—the polymerisation of styrene and the oxidation of cumene, molten polyethylene,

¶ Calculated from results obtained by Bamford, Dewar, and Burnett, cited in Ref. 15.

† Rate constants for cumene taken from Ref. 48 coincide within the limits of accuracy indicated with the constants obtained by other workers[27].

and solid polypropylene—can be represented by the same general scheme (reactions 1–3), so that the same criteria are used to assess the effectiveness of test compounds. A general criterion is the ratio W/W_X of the reaction velocities in the absence and in the presence of the compound. For inhibitors this ratio is related to the kinetic parameters of the model reactions by Eqn. (9). The minimum value at which the test compound is a potential stabiliser can be taken as $fk_{p21} = 100\ M^{-1}\ s^{-1}$, which is roughly 10% of the inhibition rate constants for weak inhibitors[14,27]. Antioxidants possessing little inhibiting activity may be of interest if they decompose hydroperoxides as well as terminating chains[33].

Quantitative assessment of thermostabilisers can be based on the macromolecular polymerisation of methyl methacrylate and acrylonitrile to high degrees of conversion[39], at which the lifetimes of the radicals R· amount to tens of minutes. Thus a certain concentration of these radicals can be produced relatively simply (by photoinitiation and by thermal initiation), and then the kinetics of their decay on the test compound

$$-\frac{d[R^{\cdot}]}{dt} = k_z[R^{\cdot}][InH].$$

can be observed. Integration of this equation yields

$$\ln\frac{W_0}{W} = k_z[InH]t, \qquad (12)$$

in which W_0 is the rate of the reaction in the absence of the test compound and W the rate of reaction at time t after cessation of initiation. This shows that the inhibition rate constant k_Z can be determined directly from the measured reaction rates W and W_0. The techniques of the accelerated testing of polymers have been described in the literature[3,20,21,53–58].

V. EXPERIMENTAL RESULTS OBTAINED BY TEST SCHEME

The effectiveness of a series of stabilisers can be compared from experimental results obtained from model reactions on simple compounds and from accelerated tests on polymers[2]. Table 1 lists data on the oxidation of molten polyethylene and on the polymerisation of styrene in the presence of four stabilisers. The sequence of inhibiting effects is maintained, although the stabilisers interact with different active centres in each model reaction.

Table 1. Inhibiting effect W/W_X of stabilisers in the oxidation of molten polyethylene and the polymerisation of styrene*.

Stabiliser	Oxidation of molten polyethylene at 135°C (10^7W_i = 4.6 M s^{-1}) initiated by dicumenyl peroxide	Polymerisation of styrene in presence of oxygen at 100°C (10^7W_i = 4.4 M s^{-1}) initiated by butylphenyltriazen	Polymerisation of styrene at 100°C (10^7W_i = 4.4 M s^{-1}) initiated by butylphenyltriazen
Diphenylamine	2	1.5	1.0
Phenyl-2-naphthylamine (Neozone D)	10	4	1.2
2,6-Di-t-butyl-4-methylphenol (Ionol)	>100	>50	10
Methylenebis-2-(6-t-butyl-4-methylphenol (2246)	>100	>50	10

* When styrene undergoes polymerisation in the presence of oxygen, most of the R· radicals are converted into RO_2· radicals.

Table 2 gives data on the inhibiting effects of three stabilisers, obtained in a model reaction and in accelerated trials on rubbers. Stronger chain-reaction inhibitors produce longer induction periods in the oxidation of the rubber. It is evident also that the peak on the differential thermal analysis curve undergoes a larger displacement to higher temperatures in the presence of a stronger stabiliser (*NN'*-diphenyl-*p*-phenylenediamine). Thus results obtained on a model reaction agree well with those of accelerated trials of these stabilisers on polymers.

Table 2. Comparison of inhibiting effects of stabilisers on a model reaction and in accelerated tests on polymers.

Stabiliser	W/W_X in polymerisation of styrene in presence of oxygen at 100°C (10^7W_i = 4.4 M s^{-1}) initiated by butylphenyltriazen	Induction period in the oxidation of SKS-30ARK rubber at 130°C, min	Shift ΔT of peak on d.t.a. curve for SKD rubber
2,6-Di-t-butyl-4-methylphenol (Ionol)	>50	760	–
NN'-Diphenyl-*p*-phenylenediamine	50	390	83
Phenyl-2-naphthylamine (Neozone D)	4	200	9

Table 3. Comparison of rates of decomposition of cumene hydroperoxide for several stabilisers with their antioxidant behaviour in rubber.

Stabiliser	Ratio W_XW of rates of decompn. of cumene hydroperoxide in presence and in absence of stabiliser at 130°C	Induction period in oxidation of SKI–3 rubber at 130°C
NN'-Di-2-naphthyl-*p*-phenylenediamine (Age-Rite White)	1.0	900
NN'-Diphenyl-*p*-phenylenediamine	1.1	900
N-Isopropyl-*N'*-phenyl-*p*-phenylenediamine (4010)	1.8	780
Methylenebis-2-(6-t-butyl-4-methylphenol) (2246)	3.0	360
Trisnonylphenyl phosphite (Polyguard)	30	48

Table 3 compares data on the rates of decomposition of cumene hydroperoxide in the presence of several stabilisers with their effectiveness (based on the induction period) as antioxidants for rubber. This induction period is found to decrease with increase in the rate of decomposition of the hydroperoxide. The stabilising effects of these compounds are evidently based solely on the ability to terminate chains in the oxidation of rubber. In respect of hydroperoxide decomposition the compounds are catalysts of rubber oxidation. For this reason methylenebis-2-(6-t-butyl-4-methylphenol) is a weaker stabiliser (according to the induction period) than is *NN'*-diphenyl-*p*-phenylenediamine, in spite of having a larger inhibition parameter in the model polymerisation of styrene (Tables 1 and 2).

Thus the experimental results obtained in the above scheme of testing show good correlation between test data on model reactions and accelerated trials of chemical compounds on polymers. This permits the use of model

reactions for the rapid selection of potential stabilisers from a large number of test compounds. Furthermore, as already noted, model reactions yield information on the mechanism of the stabilising effect in terms of primary reactions.

The results indicate also a correlation between accelerated trials on stabilisers and their stabilising effects in polymers under natural conditions. Thus the test results show that derivatives of *p*-phenylenediamine should be most effective antioxidants, as is indeed observed with most rubbers[22].

VI. QUANTITATIVE RESULTS ON ANTIOXIDANT STABILISERS OBTAINED BY MEANS OF MODEL REACTIONS

Consideration has been given[3] to optimum reaction conditions for the model initiated oxidation of cumene permitting by means of Eqn. (9) the evaluation of fk_7 (fk_{p21}) in the range 10^2–10^5 M^{-1} s^{-1} at 40, 60, and 80°C. If the stabiliser is an inhibitor and is consumed only in terminating chains, the duration of its action (the induction period) is

$$\tau = \frac{f\,[\mathrm{InH}]}{W_i} \quad . \tag{13}$$

This formula can be used to find the coefficient f from the experimental induction period. For any time t we can write

$$\frac{f\{[\mathrm{InH}]_0 - [\mathrm{InH}]\}}{W_i} = t \quad . \tag{14}$$

Substituting in (8) for [InH] from (14) and integrating, we obtain for the early stages of conversion the relation[59]

$$\frac{[O_2]}{[RH]} = -\frac{k_3}{k_7}\ln\left(1 - \frac{t}{\tau}\right), \tag{15}$$

where k_3 (k_{p11}) is the rate constant of chain propagation.

Table 4. Rate constants k_7 for reaction of peroxy-radicals with inhibitors and inhibition coefficients f.

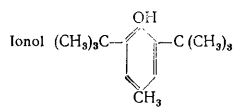
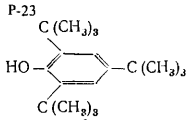
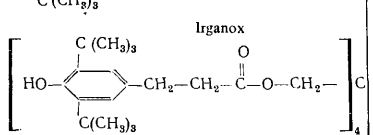
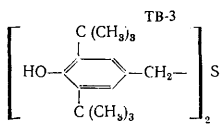
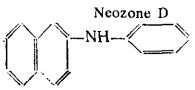
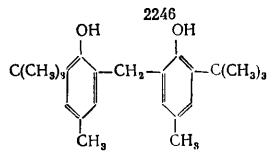
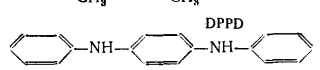
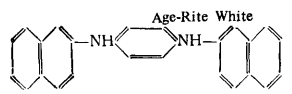
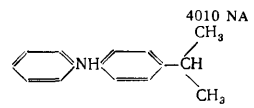
Inhibitor	Peroxy-radical	Temp., °C	lg [(k_7)60°C, M^{-1} s^{-1}]	Pre-exponential factor, lg A	E, kcal mole^{-1}	f per independent inhibiting group
Ionol 	cumene	40–80	4.34±0.03	7.27±0.32	4.46±0.49	2.1±0.1
P-23 	»	»	4.33±0.02	7.25±0.18	4.46±0.28	2.1±0.2
Irganox 	»	»	4.17±0.03	7.23±0.32	4.68±0.49	2.1±0.2
TB-3 	»	»	4.26±0.03	7.30±0.31	4.63±0.47	2.4±0.1
Neozone D 	»	»	4.83±0.03	7.03±0.39	3.34±0.60	2.0±0.2
2246 	»	»	5.60±0.05	7.09±0.66	2.28±1.0	2.0±0.1
DPPD 	»	»	5.34±0.09	—	—	2.0±0.1
Age-Rite White 	»	»	5.44±0.08	—	—	2.2±0.3
4010 NA 	»	»	5.83±0.05	7.32±0.64	2.77±0.98	2.0±0.04

Table 4 (contd.)

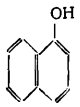
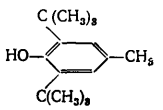
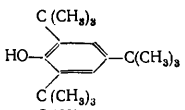
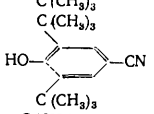
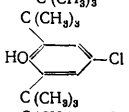
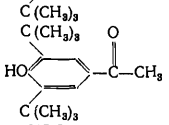
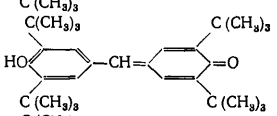
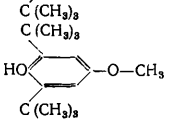
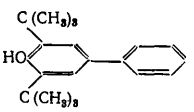
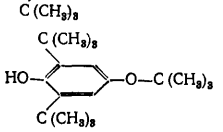
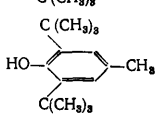
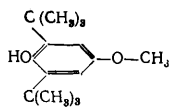
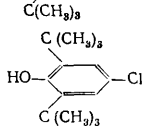
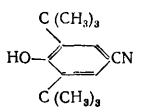
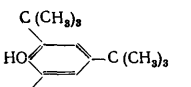
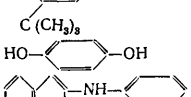
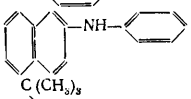
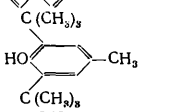
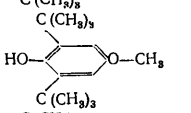
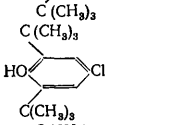
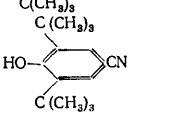
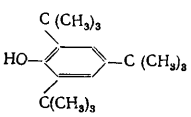
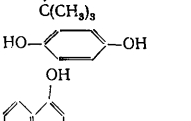
Inhibitor	Peroxy-radical	Temp., °C	lg [(k_7)60°C, M^{-1} s^{-1}]	Pre-exponential factor, lg A	E, kcal mole^{-1}	f per independent inhibiting group
	»	»	5.27±0.04	—	—	2.1±0.2
	»	»	5.29±0.09	—	—	2.0
	ethylbenzene*	40—70	4.31±0.02	7.52±0.22	4.90±0.33	—
	ethylbenzene*	40—70	4.19±0.02	6.90±0.12	4.12±0.18	—
	»	»	3.19±0.03	6.80±0.12	5.64±0.18	—
	»	»	3.92±0.02	7.20±0.12	5.00±0.18	—
	»	»	3.34±0.02	7.22±0.13	5.92±0.20	—
	»	»	4.45±0.02	7.0±0.18	3.90±0.28	—
	»	»	5.19±0.02	7.53±0.17	3.57±0.26	—
	»	»	4.27±0.03	7.48±0.33	4.90±0.50	—
	»	»	4.69±0.03	7.54±0.26	4.37±0.39	—
	styrene	13—50	4.25	—	—	—
ditto	»	»	$(4.25)_{65°C}$	—	—	—
	»	»	$(4.89)_{65°C}$	—	—	—
	»	»	$(3.83)_{65°C}$	—	—	—
	»	»	$(3.23)_{65°C}$	—	—	—

Table 4 (contd.)

Inhibitor	Peroxy-radical	Temp., °C	lg [(k_7)60°C, M^{-1} s^{-1}]	Pre-exponential factor, lg A	E, kcal mole^{-1}	f per independent inhibiting group
	styrene	13—50	$(4.21)_{65°C}$	—	—	—
	»	»	$(5.31)_{65°C}$	—	—	—
	»	»	$(4.70)_{65°C}$	—	—	—
	tetralin	50	4.43	—	—	—
	»	65	4.95	—	—	—
	»	65	3.92	—	—	—
	»	65	3.20	—	—	—
	»	»	4.45	—	—	—
	»	50	4.88	—	—	—
	»	50	4.86	—	—	—

* Experiments made in chlorobenzene with an equal volume of ethylbenzene.

Investigation of several known stabilisers in the model oxidation of cumene established that the rate curves for the absorption of oxygen in their presence are well linearised when plotted in the coordinates of Eqn. (15). This implies that the stabilisers inhibit the reaction in conformity with the simple scheme considered above‡. Hence the coefficients f and the inhibition rate constants can be determined by means of Eqns. (13) and (15). Table 4 lists values of k_7 and f for the stabilisers studied (rate constants were computed per inhibiting group). It includes for comparison values of k_7 obtained for various antioxidants on reaction with peroxy-radicals of ethylbenzene[61], styrene, and tetralin[27,*]. The inhibition coefficient f per independent inhibiting group is ~2 for all the stabilisers. This means that radicals formed from antioxidants react only with peroxy-radicals of cumene and do not interact.

Comparison of the rate constants for the reaction of any one inhibitor (2,6-di-t-butyl-4-methylphenol, its three derivatives in which the 4-methyl has been replaced by cyano, chloro, and methoxy; tri-t-butylphenol, *N*-phenyl-2-naphthylamine, 1-naphthol, or quinol) with various peroxy-radicals shows that k_7 is almost independent of the structure of the latter, as already noted above. The maximum difference does not exceed a factor of two, which may be largely due to experimental error, since the values of k_7 under comparison were obtained by different methods. Such independence of k_7 is of great interest in connection with testing, since it permits the choice of model reactions that have been most thoroughly studied and that are simplest to conduct.

Comparison of the rate constants k_7 for *para*-substituted 2,6-di-t-butylphenols shows a slight variation in reactivity of the inhibitor with the structure of the substituent provided that the latter contains an alkyl group directly attached to the benzene ring. The maximum deviation from the mean rate constant ($10^{4.30}$ at 60°C) does not exceed 30–70%. With the peroxy-radicals of cumene and ethylbenzene, for which rate constants have been determined most accurately, the maximum deviation from the mean ($10^{4.27}$) does not exceed 25%. Inspection of published data[27] shows that the rate constants k_7 obtained for various peroxy-radicals and derivatives of phenol having analogous *para*-substituents also have closely

‡This result is not self-evident, since inhibited oxidation has in general a complicated mechanism. A detailed survey has been made[60] of the general scheme of inhibited oxidation and published experimental results.

similar values (independently of other alkyl substituents). Only 7 of the 60 values of k_7 cited in Ref. 27 exhibit deviations from the mean exceeding a factor of 2.5, and the mean rate constant ($10^{4.35}$ at 60°C) is almost identical with the mean for 2,6-di-t-butylphenol derivatives.

Considerable variation in the rate constant k_7 is observed only in the presence of strong electron-donating or -accepting substituents[61]. Thus the σ-constants for 4-methoxyl, 4-cyano, and 4-methyl are respectively −0.776, +0.628, and −0.170. According to Table 4 the rates of reaction of the peroxy-radical of ethylbenzene with 2,6-di-t-butylphenol containing in the 4-position respectively hydroxymethyl, methyl, and cyano are in the ratios 100 : 10 : 1. Jaffe's well known review[62] gives σ-constants for many *p*-alkyl substituents and for various *para*-substituents with the alkyl directly attached to the benzene ring. The maximum difference in the σ-constants of these substituents does not exceed 0.5, which corresponds to an approximately sixfold difference in rate constants k_7 or a deviation from the mean by a factor of 2.5.

Thus the variation in the σ-constants for derivatives of phenol *para*-substituted with groups having weak donor–acceptor properties corresponds on the whole to the variation in the rate constants k_7. It is noteworthy that the pre-exponential factors in the inhibition rate constants are almost identical within the limits of experimental accuracy independently of the structure of the peroxy-radical or the nature of the antioxidant. Thus in reactions with peroxy-radicals of cumene and of ethylbenzene these factors are respectively $10^{7.21\pm0.11}$ and $10^{7.25\pm0.27}$. We can write for both series the general formula

$$k_7 = 10^{7.23\pm0.19}e^{-E/RT} \qquad (16)$$

for the inhibition rate constant, where 0.19 gives the standard deviation. We can use (16) to determine the activation energy if we know the rate constant at a single temperature; an error of a factor of two in this rate constant gives an error in the activation energy of only ±0.5 kcal mole^{-1}. Twelve inhibition rate constants are known[27] for the reaction of phenols with various peroxy-radicals. The mean pre-exponential factor in these constants is $10^{7.20}$, which coincides within the limits of experimental accuracy with the above value in Eqn. (16). This fact strongly suggests that experimental error is responsible for the compensating effect in these reactions observed between the pre-exponential factor and the activation energy[27], reaching 2 kcal mole^{-1} (more than a factor of ten in the pre-exponential factor).

Table 5. Rate constants of gas-phase radical substitutions involving relatively large radicals and molecules.

Reaction	Pre-exponential factor, lg (A, M^{-1} s^{-1})	E, kcal mole^{-1}
$NO+O_3 \rightarrow NO_2+O_2$	8.83±0.15	2.45±0.17
$C_2HCl_4+Cl_2 \rightarrow C_2HCl_5+Cl$	8.71±0.03	5.15±0.03
$C_2H_3Cl_2+Cl_2 \rightarrow C_2H_3Cl_3+Cl$	8.78±0.03	0.96±0.04
$CH_3+CH_3CHO \rightarrow CH_4+CH_3CO$	8.86±0.16	7.50±0.30

Hardly any sufficiently accurate data have yet been published on rate constants for other radical substitutions in the liquid phase. Only two rate constants of chain propagation can be cited, for the liquid-phase oxidation of cumene and ethylbenzene: the first was given[48] as $10^{6.67\pm0.26}\exp[-(9800\pm400)/RT]$; the second can be obtained from the refined value[63] of the recombination rate constant for peroxy-radicals of ethylbenzene[61] as $10^{6.64\pm0.24}\exp[-(9550\pm360)/RT]$. The two constants have the same pre-exponential factor, differing from that in formula (16) by only slightly more than the experimental error.

A considerably greater quantity of accurate data are available on rate constants for radical substitution in the gas phase[64]. Table 5 gives the most accurate values for reactions involving relatively large radicals and molecules. The pre-exponential factors evidently coincide within the limits of experimental accuracy. The rate constant can in general be written

$$k = 10^{8.80\pm0.07}e^{-E/RT}. \qquad (17)$$

If the frequency of collisions in the gas is taken to be 2×10^{11} M^{-1} s^{-1},[65] the steric factor becomes 0.003. If we write the reaction rate constant in the logarithmic form

$$E = \theta \lg A - \theta \lg k, \qquad (18)$$

where $\theta = 0.004575\,T$ kcal mole^{-1}, and compare the resulting expression with the well known Polanyi–Semenov relation

$$E = B \pm \alpha Q,$$

we obtain, with a constant pre-exponential factor, the general formula

$$k = Ae^{-\frac{B}{RT}}e^{\pm\frac{\alpha Q}{RT}}, \qquad (19)$$

for the rate constant, where $A\exp(-B/RT)$ is the exchange rate constant ($Q = 0$). The relation linking the rate constant with the heat of reaction may be satisfied for reactions in which the pre-exponential factor and the coefficient α are constant. For a series of reactions involving the same radical, with the resonance energy of the radicals neglected, Eqn. (19) can be written in the form

$$\pm(D_0 - D) + \frac{\theta}{\alpha}\lg k - \frac{\theta}{\alpha}\lg k_0 = 0, \qquad (20)$$

where D and D_0 are the bond energies for the abstractable atom in the series of reactions and for exchange ($Q = 0$) in this series, and k_0 is the exchange rate constant. It follows from (20) that a linear dependence should exist between the logarithm of the rate constant and the bond energy. This is supported by published data.

The diagram illustrates results obtained[61] for the rate constants of reactions of the peroxy-radical of ethylbenzene with sterically hindered phenols (Table 4) and the energies of the hydrogen–oxygen bond in the latter (line *1*), together with corresponding results for reactions of the sodium atom with chlorinated methanes (involving detachment of a chlorine atom and formation of sodium chloride) (line *2*), reaction rate constants for the latter series and carbon–chlorine bond energies being taken from Refs. 64 and 66. Both series comprise exothermic reactions, so that formula (20) becomes

$$D = D_0 - \frac{\theta}{\alpha}\lg k + \frac{\theta}{\alpha}\lg k_0. \qquad (21)$$

The diagram shows good agreement between experimental results and Eqn. (21). The slopes of the straight lines show that α has the values 0.40 and 0.65 for reactions of the peroxy-radical with phenols and for those of sodium with chlorinated methanes respectively. The intercepts made on the D-axis give bond energies of 94 and 96 kcal mole^{-1}: the former is close to the estimate[8] of 90 kcal

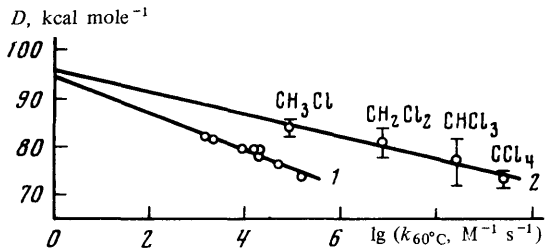
mole^{-1} for the hydrogen–oxygen bond energy in ethylbenzene hydroperoxide; the latter is almost identical with the sodium–chlorine bond energy[66] of 97.6 kcal mole^{-1}. These facts suggest that the exchange rate constants at 60°C for

$$RO^{\cdot}_2 + ROOH \rightarrow ROOH + RO^{\cdot}_2$$

and

$$Na + NaCl \rightarrow NaCl + Na$$

differ insignificantly from unity.



Linear relation between logarithm of rate constant at 60°C and bond energy of atom abstracted for series of radical substitutions of the same type: 1) liquid-phase reactions of the peroxy-radical of ethylbenzene with *para*-substituted 2,6-di-t-butylphenols; 2) gas-phase reactions of the sodium atom with chlorinated methanes.

Not all radical substitutions involving relatively large species have the above constant pre-exponential factors. In the liquid phase, for example, the rate constants for reaction of the diphenylpicrylhydrazyl radical with phenols[67] have factors of $10^{3.8-4.5}$, only one-thousandth of that in Eqn. (16). A low pre-exponential factor ($10^{3.2}$) is observed also in exchanges between sterically hindered phenoxy-radicals and phenols[67]. The low values evidently cannot be attributed to experimental error.

VII. QUANTITATIVE ASSESSMENT OF INHIBITORS IN VARIOUS COMPOSITIONS

Methods for the preliminary assessment of inhibitors on model reactions may be of general interest, since the kinetic characteristics obtained for the test compounds may be used in the investigation of chain processes occurring in hydrocarbons, foodstuffs, liquid perfumes, animal organisms, and plants. In the investigation of various compositions containing inhibiting agents it is possible to estimate the concentration of the inhibitor, establish the mechanism of its action, and determine the inhibition rate constant. Inhibitors present in lipid extracts of leaves and in petroleum have been analysed by means of the model oxidation of cumene[68,69]. Two inhibitors have been found in plants, with inhibition rate constants k_7 of 4000 and 120 000 M^{-1} s^{-1}; the second appears in the plant as winter approaches. The concentration of inhibitor—more precisely the value of $f[InH]$—in the dry extract is 0.06–0.3 mole kg^{-1}. Analysis of Western Siberian petroleum reveals four inhibitors, having inhibition rate constants of (30, 7.6, 1.4, and 0.73) $\times$ 10^4 M^{-1} s^{-1} and corresponding values of $f[InH]$ of 0.020, 0.015, 0.015, and ~0.015 mole kg^{-1}; the first three of these inhibitors are found in the asphaltenes, and the fourth occurs in the tars.

Thus both foliage and petroleum contain relatively high concentrations (0.01–0.1 mole kg^{-1}) of inhibitors. The most effective of these (with an inhibition rate constant of ~10^5 M^{-1} s^{-1}) can be assigned to the class of strongest inhibitors—antioxidants.

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Phenols as Sources of Radicals in Biochemical Systems

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The principal radical products of the initial stages of the autoxidation of phenols in polar media are examined. Attention is concentrated on the characteristics of superoxide radicals in connection with their toxic properties and important role in certain biochemical processes. The possible contribution of the radical products of the autoxidation of phenols to the mechanism of their antitumour activity is discussed.
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I. INTRODUCTION

In 1956–1957 Emanuel' put forward for the first time the hypothesis that, in principle, inhibitors of radical reactions might be used to treat certain diseases, the occurrence and the development of which may be attributed to either the appearance of free radicals which are not characteristic of the organism under normal conditions or to the breakdown of the regulation of the radical reactions occurring in the organism under the conditions of normal metabolism[1–4]. The limitations associated with toxicity led to the isolation of relatively non-toxic alkylphenols and certain polyphenols and hydroxypyridines from the large group of compounds known in chemistry as inhibitors. Comprehensive studies have been made on the carcinolytic and antitumour activities of these substances under Emanuel''s supervision.

Considerable experience has been gained in modern biochemistry concerning studies on the metabolism and physiological activities of natural and synthetic phenols in the living organism. The results of this research have been compiled mainly in a series of collected volumes and monographs[5–8]. Among the pharmacological preparations used at present, phenolic compounds are widely represented. However, it is by no means always possible to discover any relation between the pharmacological activity of a preparation and the presence of a phenolic hydroxyl in its molecule.

A significant fraction of the radicals arising in the organism under normal conditions appears to comprise radical intermediates formed from the cofactors of oxidation-reduction enzymes in the process of their functioning. In the majority of the enzymes such radicals are firmaly bound to the active centres, as a result of which they are incapable of participating in non-specific free-radical reactions. However, the formation of superoxide radicals—the products of one-electron reduction of oxygen capable of initiating chain reactions in solution—has been demonstrated in a number of enzyme systems[9]. Such systems are apparently of interest from the standpoint of the possibility of inhibiting their action with the aid of free-radical reaction inhibitors.

The ability of phenols and other compounds to inhibit free-radical reactions is known to be associated with the presence in their molecules of a relatively weak bond (60–70 kcal mole^{-1}) which enables the inhibitor to participate readily in exchange reactions with the system radicals to form inactive radicals[10,11]. Emanuel' and coworkers[12] showed that the radicals arising in proteins under the influence of radiation can react in a similar manner directly with an inhibitor molecule, forming an inhibitor radical.

On the other hand, owing to the presence of the weak bond, the inhibitor readily undergoes autoxidation. Free radicals, which can react with cell components, damaging them, and can be involved in metabolic processes, arise in the system under these conditions. The present review deals with this aspect of the action of phenolic inhibitors of free-radical reactions.

II. RADICAL PRODUCTS OF THE AUTOXIDATION OF PHENOLS IN POLAR MEDIA

The formation of relatively stable semiquinone radical-anions is characteristic of the oxidation of phenols in polar media. As in other radical reactions of phenols, the autoxidation process involves a rearrangement of the aromatic bond systems into a quinolid system with formation of cyclohexadienones (phenol–dienone rearrangements) and conversely dienone–phenol rearrangements also take place. The intermediate molecular autoxidation products (quinones) accelerate the oxidation process, the rate of which at advanced stages is determined by the characteristics of the reduction of the quinone[13–15]. The main radicals formed in the initial stages of the autoxidation of phenol are phenoxy-radicals PhO$^{\cdot}$, superoxide radical-anions $O_2^{\cdot-}$ and semiquinones $SQ^{\cdot-}$.

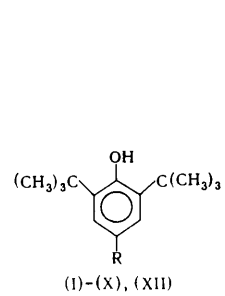
1. Phenoxy-radicals and Semiquinones in Autoxidation Processes

The autoxidation of phenols in alkaline media apparently begins with the fundamental reaction

$$PhO^- + O_2 \rightarrow Ph\dot{O} + O_2^{\cdot-} . \qquad (1)$$

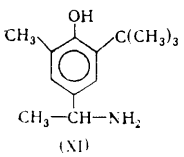
In view of the short lifetime of phenoxy-radicals in polar media[16,17], they cannot be detected by ESR under static conditions.

The kinetics of the autoxidation of sterically hindered phenols with electron-donating substituents in the *p*-position have been studied for phenols (I)–(XI).

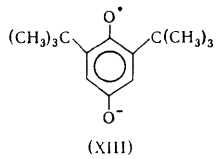


(I)–(X), (XII)

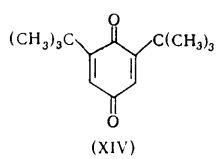
(I) R = H
(II) R = C_2H_5
(III) R = $CH_2CH(CH_3)_2$
(IV) R = CH_2Ph
(V) R = CH_3OCH_3
(VI) R = $CH_2OC_2H_5$
(VII) R = $CH_2N(CH_3)_2$
(VIII) R = $CH_2N(C_2H_4OH)_2$
(IX) R = CH_2NH_2
(X) R = CH_3CHNH_2
(XII) R = Ph



(XI)



(XIII)



(XIV)

In the oxidation of these phenols by molecular oxygen under static conditions in an aqueous alcoholic alkaline solution a radical having a triplet ESR spectrum with a splitting of 1.2–1.4 G and intensity ratios of 1 : 2 : 1 was detected. The structure of the spectrum persisted for a long time (tens of minutes) in the absence of oxygen. The kinetics of the accumulation of the radicals with the triplet spectrum were studied for phenols (VIII)–(XI).[18] The kinetic accumulation curve passes through a maximum and most of it can be described formally by the equation for first-order kinetics. Part of the curve beyond the maximum may be regarded as the kinetic curve for the consumption of the radicals. The temperature variation of the rate constant for the disappearance of the radicals was determined. For all four phenols, the activation energy obtained from this relation is 23.0 ± 0.5 kcal mole^{-1}.

The similarity of the ESR spectra and of the kinetics of the consumption of the radicals suggests that the oxidation of all the phenols investigated results in the formation of the same radical—2,6-di-t-butyl-1,4-benzosemiquinone (XIII). Its formation is characteristic of the oxidation of sterically hindered phenols with an electron-donating substituent in the *p*-position and is accompanied by the elimination of the *p*-substituent[19]. The semiquinone (XIII) is a secondary radical product formed in the initial stages of the oxidation process, probably as a result of the decomposition of an intermediate hydroperoxide with a *p*-quinolid structure—the product of the oxidation reactions of the phenoxy-radical. A detailed mechanism of the initial stages of the autoxidation of phenols has been described in a review[14].

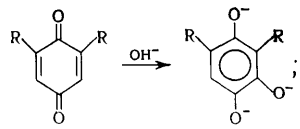
With increase of the conjugation chain and of the size of the substituent in the *p*-position, the stability of the phenoxy-radical increases. In the case of 2,6-di-t-butyl-, 4-phenyl-, and 4-naphthyl-phenols, the formation of phenoxy-radicals was observed by ESR in an aqueous alcoholic alkaline solution[20].

Direct evidence for the formation of phenoxy-radicals in the autoxidation of phenols in an aqueous alcoholic alkaline solution was obtained for phenols (VIII) and (XII)[21] by the stopped-flow method[22]. The spectra of the reaction mixture were recorded 2 s after the onset of oxidation. Absorption bands were observed for (XII) in the visible region with maxima at 428–430, 460, 480, 504, and 540 nm. Comparison of the spectrum of the reaction mixture in the oxidation of (XII) with the spectrum of (VIII) and with those of various phenoxy-radicals in polar media (results obtained by pulse photolysis and pulse radiolysis[17,23–25]) leads to the conclusion that the 428–430 nm band corresponds to the absorption of the phenoxy-radical.

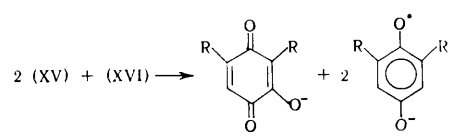
The spectrum of the reaction mixture of phenol (VIII) is more complex. In the range 430–450 nm there is a fairly broad asymmetric peak, which is probably the result of the superposition of the characteristic bands of the phenoxy-radical and the semiquinone (XIII), since it is known from the literature that different substituted semiquinones absorb mainly at 430–440 nm and less vigorously at 400 to 415 nm.[25–28] However, under certain conditions (0.005 M, 50°C) a spectrum with a narrow symmetric peak at 430 nm was also obtained for the reaction mixture of this phenol[21].

The formation of the phenoxy-radical is also supported by the detection in the reaction mixture obtained in the oxidation of phenols (V) and (VII) of disproportionation products of phenoxy-radicals—the corresponding methylenequinones [2,6-di-t-butyl-α-(*NN*-dimethylamino)-methylenequinone and 2,6-di-t-butyl-α-methoxymethyl-methylenequinone], which are stable in aqueous alcoholic alkaline solution. Under the influence of acid, these methylenequinones are converted into 3,5-di-t-butyl-4-hydroxybenzaldehyde, which has been found in the oxidation products of (VIII) following the addition of concentrated hydrochloric acid to the reaction mixture. 2,6-Di-t-butyl-1,4-benzoquinone (XIV)—the disproportionation product of the semiquinone (XIII)—was also found in the reaction mixture[19].

The study of the kinetics of the consumption of the semiquinone from phenol (VIII) by ESR showed that at advanced stages of the process an appreciable increase of the concentration of the radicals begins. When oxygen is supplied to the system after the attainment of the maximum concentration of radicals, the latter are initially almost instantaneously destroyed, after which their concentration increases sharply. This form of kinetic curve can be accounted for by the fact that the quinone (XIV), accumulating at advanced stages, is reduced and one of the reduction products is the semiquinone (XIII).[19] In the reaction of quinones with OH^- via a nucleophilic substitution mechanism the quinone is reduced to the semiquinone and *o*-hydroxyquinone should then accumulate in the system[29,30]. The principal reaction stages can be formulated as follows for alkyl-*p*-benzoquinones as an example:



(XV) (XVI)



The formation of 2,6-di-t-butyl-3-hydroxy-1,4-benzoquinone was demonstrated in the oxidation of 2,6-di-t-butyl-4-(β-hydroxyethyl)aminomethylphenol. The structure of the *o*-hydroxyquinone was demonstrated by infrared spectroscopy, ESR, and NMR. Its formation was also

demonstrated in the direct interaction of the corresponding quinone with alkali [19].

According to the ideas of Blyumenfel'd and coworkers [31,32], the primary step in the reduction of the quinone is direct electron transfer from OH^- to the quinone:

$$X + OH^- \rightleftarrows SQ^{\cdot-} + \dot{O}H, \quad (2)$$

after which the $\dot{O}H$ radicals interact with the initial quinone to form the hydroxyquinone.

The physicochemical properties and reactions of phenoxy-radicals and semiquinones have been described in detail in reviews and monographs (see Khudyakov and Kuz'min's review [25] with its bibliography).

2. Superoxide Radical-anions and an Enzymatic Method for the Investigation of Their Role in Autoxidation Processes

The formation of a phenoxy-radical as a result of the transfer of a single electron to an oxygen molecule leads to the formation of the superoxide radical-anion $O_2^{\cdot-}$, which is highly reactive. The absorption spectrum of the superoxide radical-anion, obtained by pulse radiolysis, has a maximum at 240–250 nm in aqueous solution, the extinction coefficients having widely different values according to different investigators [33,34]; $\epsilon_{O_2^{\cdot-}} = 1950 \pm 50$ litre mole^{-1} cm^{-1} appears to be the most probable value [34]. The application of the "fast freezing technique" [35] made it possible to obtain the ESR spectrum of the $O_2^{\cdot-}$ radical-anions in frozen aqueous solution; the radical-anions were formed with the aid of various chemical and enzymatic systems for the reduction of molecular oxygen; $g_\perp = 2.0$ and $g_\parallel = 2.08-2.09$. [35,36] The ESR spectrum of $O_2^{\cdot-}$ in anhydrous acetonitrile is similar to its spectrum in a frozen aqueous solution, but differs significantly from the spectrum in anhydrous dimethylformamide [37].

In aqueous solution the $O_2^{\cdot-}$ radical-anion is in equilibrium with $H\dot{O}_2$:

$$O_2^{\cdot-} + H^+ \rightleftarrows H\dot{O}_2, \quad (3)$$

whose $pK = 4.88 \pm 0.1$. [38,39] The rate constants for the recombination of $H\dot{O}_2$ and $O_2^{\cdot-}$ and for the cross-recombination are 7.6×10^5, $<10^2$, and 8.5×10^7 litre mole^{-1} s^{-1} respectively [39]:

$$H\dot{O}_2 + H\dot{O}_2 \rightarrow H_2O_2 + O_2, \quad (4)$$

$$O_2^{\cdot-} + O_2^{\cdot-} + 2H^+ \rightarrow H_2O_2 + O_2, \quad (5)$$

$$H\dot{O}_2 + O_2^{\cdot-} + H^+ \rightarrow H_2O_2 + O_2. \quad (6)$$

The $O_2^{\cdot-}$ radical-anion is an intermediate in the reduction of oxygen and can behave both as an oxidant and as a reductant depending on the composition of the reaction mixture. According to the latest data, the redox potential $E_0(O_2/O_2^{\cdot-}) = -0.33 \pm 0.01$ V, while $E_0' = 0.94 \pm 0.02$ V was obtained for the $O_2^{\cdot-}/H_2O_2$ system at pH 7. [40,41]

There are data showing that spontaneous dismutation of $O_2^{\cdot-}$ leads to the formation of $^1\Delta g$ singlet oxygen [42,43].

The formation of hydrogen peroxide is characteristic of the oxidation of phenols [44]. In the presence of H_2O_2 the reaction

$$O_2^{\cdot-} + H_2O_2 \rightarrow O_2 + OH^- + \dot{O}H \quad (7)$$

can take place [45] (by analogy with the reaction proposed for Fenton's reagent [46]). In this case hydroxy-radicals are generated together with the superoxide radical-anions in the system where phenol undergoes autoxidation.

Reaction (2) of the quinone with OH^- to form the semiquinone, discussed in Subsection 1, may be accompanied also by the reduction of quinones by the $O_2^{\cdot-}$ radical-anions with formation of the semiquinone:

$$X + O_2^{\cdot-} \rightleftarrows SQ^{\cdot-} + O_2. \quad (8)$$

The rate constants for the forward reaction (8), obtained by pulse radiolysis for a number of quinones are listed in Table 1.

Table 1. The rate constants for the reactions $X + O_2^{\cdot-} \rightarrow SQ^{\cdot-} + O_2$ involving different quinones in aqueous solution containing 5 M isopropyl alcohol and 1 M acetone [27].

Quinone	$10^{-9}k_8$, litre mole^{-1} s^{-1}
p-Benzoquinone	1.0
2-Methylbenzoquinone	0.76±0.1
2,3-Dimethylbenzoquinone	0.45±0.1
2,5-Dimethylbenzoquinone	0.36±0.1
2,6-Dimethylbenzoquinone	0.58±0.1
Duroquinone	0.005
Vitamin K	<0.0002
2,3-Dimethylnaphthoquinone	0.004
Cytochrome *c*	0.0001

The equilibrium constants K_C for duroquinone, vitamin K, and 2,3-dimethylnaphthoquinone are $(2.3 \pm 0.2) \times 10^{-2}$, $<10^{-3}$, and 2×10^{-2} respectively [27].

The use of the enzymes catalase and superoxide dismutase to investigate autoxidation in aqueous solutions established the important role of the $O_2^{\cdot-}$ radical-anions in the autoxidation of a wide variety of organic compounds: catecholamines [47–49], 6,7-dihydroxytryptamine and dialuric acid [49], pyrogallol [50], reduced flavins [51], tetrahydropteridines [52], reduced phenazine metasulphate [53], thiols [54], and inorganic sulphite [55].

Catalase catalyses the decomposition of hydrogen peroxide via the reaction

$$2H_2O_2 \rightarrow 2H_2O + O_2 \quad (9)$$

and superoxide dismutase catalyses the dismutation of the $O_2^{\cdot-}$ radical-anions via reaction (5). [56]

The conclusions reached concerning the role of H_2O_2 in the oxidation of catecholamines on the basis of the influence of catalase on this process are extremely contradictory [47–49,57]. The discrepancies between the results are probably due to the inadequate purity of the catalase preparations, which may contain an admixture of superoxide dismutase [58]. The problem of the contribution of reaction (7) and of the role of $\dot{O}H$ radicals in autoxidation process therefore remains open.

The leading role of the $O_2^{\cdot-}$ radical-anions in autoxidation processes can be demonstrated by the following examples. When superoxide dismutase is added to a system in which 6-hydroxydopamine undergoes autoxidation at pH 7.4–9.0, the rates of formation of the quinone and of absorption of oxygen decrease by 83 and 73% respectively [48]. In the oxidation of epinephrine to adrenochrome at pH 10.2, the inhibition reaches about 80% [47] and in the autoxidation of pyrogallol at pH 7.9–9.1 it ranges from 99 to 90%. [50]

The inhibition of autoxidation in the presence of superoxide dismutase can probably be accounted for by the suppression of reactions (8), (10), and (11):

$$PhO^- + O_2^{\cdot-} \xrightarrow{H^+} PhO^{\cdot} + H_2O_2 , \quad (10)$$

$$SQ^{\cdot-} + O_2^{\cdot-} \xrightarrow{H^+} X + H_2O_2 . \quad (11)$$

The dependence of the degree of inhibition on the pH of the medium, which is not related to the stability of superoxide dismutase, is noteworthy. For pyrogallol, the inhibition is more pronounced at pH < 10, while for epinephrine or tetrahydropteridines it is actually more marked at pH > 8.5, decreasing as the pH is reduced.

This apparently indicates the occurrence of two oxidation mechanisms, only one of which is associated with a significant role of the $O_2^{\cdot-}$ radical-anion. The predominance of one of these mechanisms depends on specific conditions.

After a new method is discovered, a period of its intensive application usually begins, in which the limitations of the method are not always taken into account. In view of this, some data concerning the characteristics of autoxidation in the presence of superoxide dismutase are given below.

Autoxidation reactions are extremely sensitive to traces of variable-valence metals, which have a significant influence on the rate and mechanism of the process. In the presence of Cu^{2+}, Mn^{2+}, and Fe^{2+} ions superoxide dismutase does not inhibit the oxidation of pyrogallol. The influence of metal ions is eliminated in the presence of diethylenetriaminetetraacetic acid, while ethylenediaminetetraacetic acid (0.001 M) does not suppress the action of Fe^{2+} at micromolar concentrations. The $O_2^{\cdot-}$ radical-anions probably form with metal ions intermediate complexes which do not react with superoxide dismutase[50].

The absence (under certain conditions) of inhibition by superoxide dismutase of the oxidation of low-molecular-weight thiols in the presence of heavy metals is probably associated with a similar phenomenon; on this basis, the stage involving the interaction of the thiol with the $O_2^{\cdot-}$ radical-anion has been apparently erroneously excluded[54] from the mechanism of the oxidation of thiols.

Recent data have shown[59] that phenols, particularly catechols, can combine reversibly with superoxide dismutase and can interact with the metal forming part of the active centre of the enzyme via a process of the type

$$Cu^{2+} + PhO^- \rightarrow Cu^+ + SQ^{\cdot-}. \quad (12)$$

(Superoxide dismutase contains copper, zinc, manganese, or iron depending on its biological source.)[9]

It can be shown for *p*-benzosemiquinone as an example that Cu^{2+} readily forms complexes with semiquinones and the lifetime of such complexes is significantly longer than the lifetime of the semiquinones themselves (owing to the delocalisation of the electron over the electron shell of copper and the electrostatic repulsion of the complexes from one another[28]). Apparently in consequence of the elimination of reaction (11) in the presence of superoxide dismutase and of the stabilisation of the semiquinone as a result of complex formation, the steady-state concentration of semiquinones increases and in many cases, for example in the autoxidation of 1,2-dihydroxybenzene-3,5-disulphonic acid (Tiron) can exceed by two powers of ten the steady-state concentration in the absence of superoxide dismutase. The ESR spectrum of the autoxidising Tiron–superoxide dismutase system then shows a new signal, which has been attributed to a complex formed by the copper bound in the enzyme with catechol, and the intensity of the initial copper signal falls[59]. Apart from complex formation with the metal, semiquinones can also be stabilised by their non-specific sorption on the protein molecule[60-63].

Thus not only the elimination of the $O_2^{\cdot-}$ radical-anion from the system but also the stabilisation of the semiquinones can contribute to the inhibition of the phenol autoxidation process observed in the presence of superoxide dismutase. Therefore, in elucidating the role of superoxide radical-anions in autoxidation processes with the aid of superoxide dismutase, account must be taken of both the consumption of the substance being oxidised and of the accumulation of semiquinones in the system.

The study of the influence of various organic solvents on the superoxide dismutase activity showed that the highest activity (about 90% of that in aqueous solution) is observed in *N*-methylformamide. The results obtained[64] extend the scope of the application of superoxide dismutase in the study of the mechanisms of the oxidation of organic compounds.

III. OXIDATIVE INACTIVATION OF SH-CONTAINING ENZYMES

It has been shown that propyl gallate (PG), a polyphenol inhibitor of free-radical reactions, does not inhibit the reaction catalysed by lactate dehydrogenase (LDH) (approximately 10^{-4} M) following its direct addition to the reaction system. Nor is the enzyme inactivated as a result of its prolonged preliminary incubation with PG under conditions excluding the autoxidation of phenol, nor in incubation with stable phenol autoxidation products. Enzyme activity is lost only when LDH is incubated with PG under the conditions of its autoxidation. These data led to the conclusion that the inactivation is caused by the free radicals formed from PG during its autoxidation[65,66].

This conclusion was confirmed[67] in a study of the effect of PG on other enzymes acting via various mechanisms: glyceraldehydephosphate dehydrogenase (GAPD) (also an autoxidation-reduction enzyme in glycolysis)[68], aldolase (a glycolytic lyase)[69], and RNA polymerase—the enzyme involved in the synthesis of RNA on a DNA matrix[70].

The conclusion that the radical products of the autoxidation of the inhibitor exhibit inactivating activity has been confirmed by kinetic data. The activation energy for the inactivation of LDH is 8300 ± 500 cal $mole^{-1}$ and is equal to the activation energy for the autoxidation of PG under the same conditions[71]. The agreement between the activation energies for the oxidation of PG and the inactivation of the protein shows that the rate-limiting stage in the activation of the enzyme by the inhibitor is the stage involving the formation of the semiquinone and the $O_2^{\cdot-}$ radical-anion via the overall reaction

$$PG^- + O_2 + OH^- \rightarrow SQ^{\cdot-} + O_2^{\cdot-} + H_2O,$$

where PG^- is the anion derived from propyl gallate.

SH is the most reactive group in proteins. The extensive factual data on the reactivity and role of mercapto-groups in the structure and functions of proteins are contained in Torchinskii's monograph[72].

Since all the enzymes enumerated above contain SH groups, which form part of the active centre or are important for the maintenance of the native structure, it was natural to suppose that the proteins are inactivated as a result of the interaction of their SH groups with the radicals formed in the autoxidation of the inhibitor. Indeed, direct experiments showed[68,69,73] that the radical

products of the autoxidation of PG oxidise the SH groups of the proteins with formation of S–S groups. Throughout the joint oxidation of PG and the protein, the total amount of SH and S–S groups remains constant. This implies that neither radical nor molecular intermediates in the oxidation of PG add to the protein molecule via the sulphur atoms. The inability of *o*-hydroxyquinone, formed in the oxidation of PG,[74–76] to add to the SH group is probably due to the presence of a powerful electron-donating substituent (OH group) in the ring next to the unsubstituted hydrogen[77]. One cannot rule out the possibility that the inhibitors of radical processes, whose oxidation leads to the formation quinones capable of adding to the SH-groups, inactivate the SH-containing enzymes not only as a result of the oxidation of SH groups but also by the addition of the quinone to the latter.

SH-containing compounds, including proteins are known to be capable of reducing antioxidant radicals. Their synergistic activity in relation to inhibitors is in fact associated with this factor. The enhanced rate of the consumption of SH groups in the presence of an inhibitor undergoing oxidation and the appearance of an induction period on the kinetic curve for the oxidation of the inhibitor in the presence of the protein (in the absence of the protein, PG is oxidised under these conditions at a constant rate) suggest that, during the induction period in the oxidation of PG, the following reactions take place[73]:

$$PG^- + O_2 + OH^- \rightarrow SQ^{\cdot-} + O_2^{\cdot-} + H_2O;$$
$$PG^- + O_2^{\cdot-} + H^+ \rightarrow SQ^{\cdot-} + H_2O_2;$$
$$RS^- + SQ^{\cdot-} + H^+ \rightarrow PG^- + RS^{\cdot};$$
$$RS^- + O_2^{\cdot-} + 2H^+ \rightarrow RS^{\cdot} + H_2O_2;$$
$$2\,RS^{\cdot} \rightarrow RS - SR;$$
$$2\,O_2^{\cdot-} + 2\,H^+ \rightarrow H_2O_2 + O_2.$$

It has been shown for LDH[78] that the oxidation of the SH groups alters the kinetic characteristics of the enzyme: the stability of the LDH complex with the coenzyme—reduced nicotinamide-adenine dinucleotide (NADH)—is significantly reduced (the dissociation constant increases by a factor of 4–5).

Thus the decrease of the activity of enzymes as a result of their interaction with radicals proceeds not only owing to the decrease of the number of active centres but also owing to a change in the affinity of the coenzyme for the enzyme. The latter may be caused by structural changes resulting from the oxidation of SH groups to S–S, which are not characteristic of the enzyme in the intact state.

The influence of radical autoxidation products on the structure of SH-containing proteins has been demonstrated in experiments on GAPD and aldolase by the change in specific rotation. A decrease in laevorotation and, after prolonged incubation corresponding to the decrease of the enzyme activity by about 80% and the oxidation of SH groups to the extent of 50–80%, the appearance of dextrorotation are characteristic of both enzymes (Table 2).

The inactivation of the enzyme by radicals can be prevented by allowing the inhibitor to react with the enzyme in the presence of a reducing agent: NADH for LDH[71] or β-mercaptoethanol for RNA polymerase[70]. The protection of the protein from inactivation is accompanied by the oxidation of NADH to NAD^+. It is known from the literature that NADH forms a stable complex with the SH groups of LDH. The presence of this complex stabilises the protein and protects it from thermal denaturation, denaturation by urea, and the action of various agents on the SH groups.[79–83] Since in the system with PG undergoing autoxidation the protective effect of NADH is accompanied by its oxidation, the stabilisation of LDH is temporary and its duration depends on the NADH concentration. The oxidation of LDH and NADH present together in a medium containing PG undergoing oxidation obeys the general rule governing the behaviour of a mixture of two inhibitors of different strengths in autoxidation reactions[84].

Table 2. The change in the specific rotation α_{541}^{25} (degrees) of aldolase and GAPD on oxidation[68,69].

System	Duration of oxidation, min				
	0	15	30	45	60
Aldolase*	−63.0	−58.8	−48.0	—	−19.5
Aldolase*–0.001 M PG	−63.0	−26.0	—	—	+2.2
GAPD*	−37.6	−23.6	−23.6	−23.6	−23.6
GAPD*–0.001 M PG	−37.6	−17.6	−8.8	+3.1	—

*In universal buffer at pH 9.7.

The conclusion that radicals formed in the autoxidation of PG oxidise the LDH–NADH complex has been confirmed by data for the oxidation of NADH in the complex by $O_2^{\cdot-}$ radical-anions obtained by pulse radiolysis[85]. It was shown that the oxidation of NADH is a chain process. The chain length is a function of the ratio [NADH]:[LDH], the concentration $[O_2]$, the dose rate, and the pH of the medium. The maximum chain length is 9.6.

The incubation with glutathione of LDH inactivated by the autoxidation radicals does not reactivate the enzyme[73]; cysteine reactivates GAPD only under certain conditions[68]. The profound changes in the structure of the protein caused by the oxidation of the SH groups can be explained by the thiol–disulphide exchange reaction[68,73]. By analogy with the reduction of simple disulphides by mercaptans, this reaction can be treated as a result of nucleophilic attack on the disulphide linkage by the mercaptide anion:

$$R'S^- + R - S - S - R \rightarrow R'-S-S-R' + RS^-.$$

According to some investigators, this reaction can proceed via a chain mechanism and can lead to the aggregation and denaturation of proteins[86,87].

The changes in the quaternary structure of proteins as a result of the oxidation of SH groups are also indicated by data showing an increase of the bond strengths between the GAPD and aldolase subunits after incubation of these enzymes in the presence of PG undergoing oxidation[88–90]. The sorption of semiquinones[60–63] and of the phenols themselves on inactive centres of the proteins can make a definite contribution to the change in the enzyme structure. This can probably explain the influence of PG on the equilibrium between the oligomer and its subunits in the case of LDH and GAPD.[90]

The reaction of the autoxidation radicals with the SH groups of proteins is fairly selective. Thus ribonuclease and trypsin, which are proteins without SH groups, are not inactivated in the presence of PG undergoing autoxidation[68]. According to Tanksley et al.[91], the inhibition of the conversion of pepsinogen into pepsin in the presence of gossypol a naturally occurring phenol, is enhanced at

alkaline pH of the medium and with increase of temperature, which should promote the oxidation of gossypol. It was shown that, under these conditions, gossypol combines with the ϵ-amino-groups of lysine via covalent linkages.

Phenols, which behave as electron donors, readily form complexes with various acceptors, charge-transfer forces making a significant contribution to the stabilisation of the complexes. In this sense interaction with molecular oxygen can be regarded as a special case—total charge transfer via reaction (1) with formation of two free radicals. The energy of the highest occupied molecular orbital E_{HOMO} is used as a criterion of the susceptibility of phenols to oxidation[14]. In the case of charge-transfer complexes (CTC) the values of E_{HOMO} for different donors should be correlated with the stability constants of the complexes formed by the donors with the same acceptor.

The biochemically important complexes of phenols, catechols, and naphthalenediols with flavins and flavoproteins are well known[92-102]. The charge-transfer complex of naphthalene-2,3-diol and lumiflavin was isolated in a crystalline state. It was shown by X-ray diffraction that the complex has a "sandwich" structure in which the flavin molecule is located between two naphthalenediol molecules[101].

Table 3. The stability constants of the PG–FMN complexes.

Flavin	K_{st}, litre mole^{-1}	
	pH 6.3	pH 8.1
Oxidised	119	70
Reduced	$\leqslant$17	—
Half-reduced	1550	$\leqslant$20

The stability constants K_{st} of the complexes formed by PG with flavin mononucleotide (FMN) reduced to different extents have been obtained[98]. Table 3 shows that at pH 6.3 (where all the components are unionised) the most stable complex is formed with the half-reduced form of the flavin. The dependence of the stability constants of the complexes on the state of ionisation of the components and on the degree of reduction of the acceptor and also the linear relation between $\lg K_{st}$ and E_{HOMO} for FMN and various donors (Table 4) indicate a significant contribution of charge-transfer forces to the stabilisation of such complexes. It has been shown for xanthine oxidase[99,104] that the formation of complexes by phenols with flavin enzymes can lead to a significant inhibition of the enzymatic reaction.

Different aspects of the mechanism of the action of phenols on enzymes have been discussed[105]. Many phenols (mainly those with electron-accepting substituents) have been tested as uncoupling agents for oxidative phosphorylation and respiration. However, it was not possible to observe correlations between any physicochemical properties of the phenols and their uncoupling capacity. For comparison with the inhibiting activity of phenols in relation to LDH and hexokinase, the authors used, for example, the hydrophobic binding constant π and the Hammett constant σ. Of the 17 phenols investigated, 10 obey the correlation equation linear in π and σ, but the inhibition effect proved to be unrelated to the activity of the phenols as uncoupling agents. It is suggested that the uncoupling agents act directly on ATPase, forming a complex at the site of addition to the enzyme of the adenine component of the substrate[106].

It has been shown that PG also inhibits respiration and uncouples oxidative phosphorylation and respiration[107]. For phenols as inhibitors of malate dehydrogenase (an SH-containing enzyme), the correlation equation takes into account the same characteristics of the phenols (π and σ), but the equations are respectively linear and quadratic in these constants[108].

Table 4. The stability of the complexes formed by FMN with various donors and the values of E_{HOMO} for the donors (phosphate buffer, pH ~ 6).[100]

Compound	K_{st}, litre mole^{-1}	E_{HOMO} (in units of β)	References
FMNH	3.352	—0.105	103
FMN	2.000 (1.778)	0.496	103 (98)
Naphthalene-2,3-diol	2.384	0.338	96
β-Naphthol	2	0.436	93
Phenol	1.494	0.515	94
n-Propyl gallate	2.076	0.255	98

The inhibiting effect of dicumarol on respiration and phosphorylation and on the uncoupling of these processes has been attributed[109] to the direct inhibition of succinate dehydrogenase. Pyrogallol, sodium gallate, and other substituted phenols inhibit catechol methyltransferase[110-113]. The inhibition of the enzyme increases as a result of its preliminary incubation with pyrogallol[112]. It is suggested[50] that the $O_2^{\cdot}$ radical-anions and possibly OH radicals, formed by reaction (7), contribute to the inhibiting effect, particularly if one remembers that catechol methyltransferase contains "essential" SH groups.

IV. BIOCHEMICAL CHANGES UNDER THE INFLUENCE OF SUPEROXIDE RADICAL-ANIONS AND THE POSSIBLE ROLE OF THE LATTER IN THE ANTITUMOUR ACTIVITY OF PHENOLS (IN ENZYME SYSTEMS AND AT THE CELLULAR LEVEL)

A few years ago the biological role of $O_2^{\cdot}$ radical-anions was considered mainly in connection with the effect of radiation. After the discovery of superoxide dismutase[56], vigorous research was begun on the role of $O_2^{\cdot}$ in the metabolism of living organisms. It was found that the products of the one-electron reduction of oxygen ($O_2^{\cdot}$ radical-anions) are invariably present as metabolites in all plant and animal organisms and microorganisms employing molecular oxygen in their metabolic processes which have been investigated hitherto. All these organisms (no exceptions have so far been found) also contain enzymes from the family of superoxide dismutases, which catalyse selectively the dismutation of $O_2^{\cdot}$ radical-anions. The hypothesis that $^1\Delta g$ singlet oxygen is also a substrate of superoxide dismutase has been frequently discussed in the literature[43,114-116]. However, the latest data[117-120] have shown that $^1\Delta g$ oxygen is formed only on spontaneous dismutation of $O_2^{\cdot}$ and in the presence of superoxide dismutase the latter precedes the formation singlet oxygen.

Superoxide dismutase is one of the "fastest" enzymes. The rate constants for the overall second-order reaction, obtained by different investigators using various methods, agree satisfactorily [121-123]. According to the latest, improved data, $k = (2.37 \pm 0.18) \times 10^9$ litre mole^{-1} s^{-1} at 25°C, [123] which is close to the rate constants for diffusion-controlled reactions.

The system for the catalytic dismutation of $H\dot{O}_2$ radicals and $O_2^{\cdot-}$ radical-anions in the presence of Cu^{2+} in acid media can serve as a chemical model of the action of superoxide dismutase. The rate constants are about 10^8 and 8×10^9 litre mole^{-1} s^{-1} respectively [124], i.e. we have here the unique case where the reaction in the model chemical system is 3–4 times faster than in the presence of the enzyme.

The rate of reactions catalysed by superoxide dismutase is independent of the pH over a wide range of the latter (5.3–9.5). [9] The enzyme is reduced and inactivated by the final reaction product (H_2O_2). [125-128] The inactivation is a second-order reaction with a rate constant of 3.1 litre mole^{-1} s^{-1} at 20–25°C and is probably associated with the decomposition by the peroxide of one histidine residue, which is essential for activity, for each of the two polypeptide chains of the enzyme [128].

Evidently, together with catalase and peroxidase, superoxide dismutase constitutes a system for the protection of organisms from the toxic effect of oxygen and its reduction products. The system of bioantioxidants can be regarded as a second line of defence operating under conditions where enzyme systems do not work [9].

Several biological sources of $O_2^{\cdot-}$ radical-anions have now been discovered. Apart from the autoxidation reactions and the reoxidation of low-molecular-weight metabolites, mentioned in Section II, the $O_2^{\cdot-}$ radical-anions arise in the autoxidation of the oxygen adducts with haem-containing proteins: haemoglobin, myoglobin, and cytochrome R-450. [120,129,130] (For the formation of the autoxidation product of haemoglobin—methaemoglobin, an alternative mechanism of electron transfer, using external donors, particularly phenols, with intermediate formation of semiquinones from the latter, has also been suggested [131].) The electron transfer chains in plant chloroplasts [123,133], in mitochondria [116,134,135], and in microsomes [136-142] in animal organisms also function as sources of $O_2^{\cdot-}$ radical-anions. Their formation in electron transfer chains is attributed primarily to the functioning of flavin dehydrogenases [143,144].

The system in which xanthine is oxidised to uric acid, catalysed by xanthine oxidase, is the most thoroughly investigated enzymatic source of $O_2^{\cdot-}$ radical-anions [35,36,145]. During this reaction, oxygen is reduced in two stages to hydrogen peroxide. Experiments on the quenching of the chemiluminescence in the xanthine oxidase system in the presence of luminol showed that inhibitors of free-radical reactions belonging to the class of sterically hindered phenols and hydroxypyridines can behave as effective quenching agents [100], probably as a result of the capture of $O_2^{\cdot-}$ radical-anions. The binding of $O_2^{\cdot-}$ can probably also make an important contribution to the mechanism of the antitumour activity of inhibitors of free-radical reactions.

The $O_2^{\cdot-}$ radical-anions formed in electron transfer chains are involved in the peroxide oxidation of lipids and the hydroxylation of extraneous substances entering the organism (including medicinal compounds) [146-148], which are called xenobiotics. The enzyme system for the hydroxylation of xenobiotics is located in microsomes.

The detoxification of xenobiotics is attributed specifically to their hydroxylation, which leads to a decrease of their solubility in the lipid phase, hinders their passage through membranes, and facilitates their elimination from the organism. The mechanism of the functioning of the hydroxylating system has been discussed in a number of reviews [149-153].

The inhibition of the metabolism of xenobiotics by PG and other antioxidants has been demonstrated [154]; the authors explain it by the combination of the inhibitors with the flavoprotein. However, one cannot rule out the possibility that the inhibition is caused by the capture of the radicals involved in the hydroxylation processes. These radical species may be both $O_2^{\cdot-}$ and $\dot{O}H$. [140,155,156] Both types of radicals are formed also in model hydroxylation reactions [157,158]. A relation has been demonstrated between the xanthine oxidase system and the xenobiotic hydroxylation system, which includes cytochrome P-450, nicotinamide adenine dinucleotide phosphate, cytochrome *c* reductase, and the lipid component of phosphatidylcholine [159]. Xanthine oxidase is exceptionally widely distributed in living organisms. It has been recently suggested that one of the important and possibly the main function of this enzyme is catalysis by the latter of the formation of H_2O_2 and $O_2^{\cdot-}$ in the cell [160].

Studies by a number of workers have shown the existence of a direct relation between enzyme systems for the peroxide oxidation of lipids and for the hydroxylation of xenobiotics. These two systems apparently use the same electron-transport chain, as a result of which the induction of peroxide oxidation leads to a decrease of the rate of hydroxylation and conversely [161-164]. There are data concerning the existence of a factor which regulates the level of activity of these enzyme systems [142].

The radicals formed in the microsomal electron transfer chain can cause the haemolysis of erythrocytes [136,137,165], which can be averted, for example, by an increase of the level of the natural antioxidant (tocopherol) in the animals from which the erythrocytes have been taken and in the presence of superoxide dismutase and catalase. Both enzymes exhibit a similar effect, protecting mitochondrial membranes from lysis associated with the peroxide oxidation of lipids [135].

The involvement of $O_2^{\cdot-}$ radical-anions in the mechanism of the action of peroxidases has been noted in a number of studies [166,167]; the bactericidal action of the enzymes, which becomes more pronounced in the presence of phenols and epinephrine, has been attributed to these radicals [168,169] (possibly in consequence of their capacity for autoxidation with formation of $O_2^{\cdot-}$ radical-anions).

In the development of the tumour process significant changes occur in the enzyme systems for the protection of the organism from the toxic effects of the products of the peroxide oxidation of lipids (with the aid of glutathione peroxidase and glutathione reductase—enzymes governing the utilisation of lipid peroxides—and superoxide dismutase). With increase of tumour growth in the organs of the tumour-carrying animal, the activities of glutathione reductase and peroxidase pass through extrema, exceeding for a time by factors of 2.5 and 6 the corresponding levels of their activity under normal conditions, while the activity of superoxide dismutase hardly changes [170]. At the same time sharp changes are observed in the activity of the enzyme system for the peroxide oxidation of lipids [171] and peroxides accumulate [172]. The results indicate a disturbance of the balance in the processes involving the formation and utilisation of lipid peroxides, which is a characteristic link in the pathogenesis of malignant growth [170]. In the tumour itself the activities of glutathione peroxidase and superoxide dismutase, cal-

culated in terms of arachidonate (one of the principal sources of peroxides) are higher by factors of 2.5 and 12 than in the livers of intact animals. Thus the rate of formation of peroxides decreases in the tumour tissue probably in consequence of the capture of $O_2^{\cdot-}$ radical-anions by superoxide dismutase and their accelerated utilisation owing to the increased activity of glutathione peroxidase. This leads to an extremely low steady-state concentration of peroxide, which cannot be determined[170]. In chemical carcinogenesis and malignant growth the activity of the system for the hydroxylation of xenobiotics varies in opposition to the activity of the system for the peroxide oxidation of lipids[173].

The problems associated with the action of inhibitors as possible regulators of the processes occurring with participation of free radicals are outside the scope of the present review and are considered elsewhere[174].

The $O_2^{\cdot-}$ radical-anions play a significant role in phagocytotic processes. It has been shown that phagocytosis is accompanied by an increase in the rate of formation of $O_2^{\cdot-}$.[175] The bacteria *E.coli*, grown on a medium deficient in iron and with a deficiency of the iron-containing superoxide dismutase, are much more sensitive to the bactericidal action of the formed elements of blood[176]. In lymphogranulomatosis (a malignant tumour of lymphoid tissue) there is no increase of the oxidative metabolism of human leucocytes in phagocytosis[175].

The $O_2^{\cdot-}$ radical-anions can cause the degradation of the synovial (interarticular) fluid and the depolymerisation of a highly polymeric acid mucopolysaccharide contained in it—hyaluronic acid[177]. The inhibition of both processes by superoxide dismutase, catalase, and substances capable of binding ȮH radicals shows that the latter are also evidently involved in the depolymerisation and degradation processes. In inflammatory processes such as arthritis there is a distinct correlation between the number of leukocytes and the degree of degradation of the synovial fluid. These data are consistent with the finding that the synovial fluid contains superoxide dismutase and catalase at concentrations smaller by 2–3 orders of magnitude than the intracellular concentrations of these enzymes.

Since the lifetime of superoxide radical-anions is relatively long (compared, for example, with ȮH radicals), they can diffuse, in principle, within the bacterial cell and can have a lethal effect on DNA. The degradation of biomacromolecules (ribonuclease and lysine:RNA ligase) has been observed[178]. The experiments on the influence of PG undergoing oxidation on DNA have shown that the decrease of the viscosity of the DNA solutions observed in the course of incubation and the appearance of single and double breaks are due to the effect of radical and molecular inhibitor oxidation products[179]. Streptonigrin, an antibiotic with a *p*-quinonoid structure, has a similar effect on DNA when it is reduced in the presence of the latter[180] and the formation of $O_2^{\cdot-}$ radical-anions was demonstrated in this process[181]. The radiation-chemical yield of the deamination products (G) in the radiolysis of aqueous DNA solutions due to $O_2^{\cdot-}$ radical-anions is close to the value of G due to ȮH radicals[182].

The possible contribution of the radical products of the autoxidation of inhibitors to the mechanism of the antitumour action of these compounds at the cellular level can be inferred from certain indirect biochemical and cytological data quoted below. *In vivo* and *in vitro* experiments showed that inhibitors of radical reactions inhibit the synthesis of protein and nucleic acids in tumour cells[183–187], possibly as a result of the interaction of the radicals, formed in the autoxidation of the inhibitors with the SH groups of the enzymes[70]. The degree of suppression of biosynthesis increases with increase of pH in the incubation medium[186] and decreases when the aeration is inadequate[67].

PG suppresses glycolysis in tumour cells[188], which is caused, according to the data of Schön and Venker[189], by the denaturing effect of the inhibitor on the proteins. A number of inhibitors (nordihydroguaiaretic acid, butoxytoluene, ascorbyl palmitate, and octyl gallate) have been shown to block the dehydrogenase processes in the liver, which the authors explain by the oxidation of the antioxidants[190].

According to Emanuel' et al.[191], inhibitors suppress the activity of the oxidation-reduction enzymes in tumour cells. Succinate oxidase [succinate dehydrogenase?] and cytochrome oxidase are suppressed in the succinate oxidase chain of the system, the latter enzyme being more sensitive to the action of inhibitors. The degree of suppression of enzyme activity falls with increase of the overall concentration of the protein in the system (including inert protein), which indicates non-specific binding of the inhibitors to the proteins. The decrease of the degree of inhibition by an order of magnitude in the presence of a deficiency of oxygen[192] shows that the species sorbed are in all probability not the inhibitors themselves but radical or molecular products formed from them in the course of autoxidation.

Treatment with inhibitors leads to the suppression of the multiplication of tumour cells under the conditions of their growth and increases greatly the number of chromosomal aberrations, giving rise to an effect analogous to that of radiomimetic substances and free radicals[193,194]. This factor suggested[193] that the observed effects are associated with the action of the radicals formed from the inhibitors in the course of their oxidation in the cell substrate.

Substituted phenols, natural phenolic compounds, and stable radicals present at certain concentrations sensitise tumour cells to irradiation[195–200].

A separate study of the influence of inhibitors on the life cycle of cells demonstrated the blocking of phases in the cycle and the consequent disturbance of the dynamics of the cell population and a change in the distribution of the population among the different phases of the life cycle[201,202]. According to Terasinia[203] and Harris[204], certain stages in the cell cycle (the second half of the phase involving the synthesis of DNA and the end of the premitotic phase) are characterised by an increased content of SH groups. The cytotoxic action of a number of catecholamines and their polyhydroxy-analogues is attributed to the ability of these compounds to generate $O_2^{\cdot-}$ and ȮH during autoxidation. As a result of treatment with PG, tumour cells lose their capacity for transplantation and explantation[205–209].

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Bioantioxidants and Synthetic Inhibitors of Radical Processes

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Data are presented for the physicochemical characteristics of bioantioxidants and the influence on their level in the lipids of organs and tissues by radical-process inhibitors introduced into animals. A wide variety of pathological states occurring against the background of changes in the amount of bioantioxidants and the possibility of treating them with the aid of synthetic inhibitors are discussed. The effectiveness of antioxidants is associated with the important role of free-radical oxidation reactions in the lipids of cell membranes.
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I. INTRODUCTION

On the hypothesis that free-radical mechanism play a major role in the development of pathological processes, Emanuel' and coworkers suggested in 1957 that relatively non-toxic inhibitors of oxidation reactions (antioxidants) be used as protectors against radiation sickness[1]. The inhibitors were regarded as potential protective agents against radiation, capable of decreasing the scale of the damage associated with the intensification of free-radical reactions in cell components under the influence of radiation[2]. In 1957 data were obtained indicating the possibility of using inhibitors as such protective agents[1]; these results were subsequently confirmed[3-7]. However, later it proved impossible to reproduce in a number of investigations the high effectiveness of inhibitors as protective agents against radiation and in some cases it was actually found that preparations of this class intensify the effect of radiation[8]. All these findings required a more profound study of the influence of synthetic inhibitors on cell metabolism. The present author believes that the fundamental questions associated with the use of inhibitors (antioxidants) in medicine are as follows:

1. Can one assume that free-radical process inhibitors manifest in the organism the same properties as in model free-radical reaction systems and is their pharmacological activity associated with their physicochemical constants?
2. Can synthetic inhibitors and the natural antioxidants present in cell components interact and be interchanged?
3. What are the molecular-biological mechanisms of the influence of inhibitors on cell metabolism?

In the present review these questions will be considered in relation to the free-radical processes in the lipid components of the cell.

II. PHYSICOCHEMICAL CHARACTERISTICS OF BIOANTIOXIDANTS

Experiments *in vitro* showed that free-radical oxidation reactions can be suppressed in the lipid fractions extracted from animal organs and tissues[9]. The overall antioxidant activity (AOA) of the lipid fraction depends on the amount, physicochemical properties, and mutual influence of the individual antioxidants present in it, and also on the presence of substances which themselves do not exhibit antioxidant properties but can intensify or weaken the action of antioxidants[10].

It has now been shown that many substances contained in the lipids of animal organs and tissues have the properties of radical-process inhibitors. These include tocopherols, ubiquinones, steroid hormones, thyroid hormones, cholesterol, phospholipids, and certain others. The mechanism of the antioxidant action of these substances has not been established in all cases.

The most thoroughly investigated antioxidants are tocopherols, which exhibit powerful antiradical properties[11-28]. The rate constant for the reaction of α-tocopherol with free radicals k_7, measured by a chemiluminescence method in the model ethylbenzene oxidation initiation reaction at 37°C, proved to be 2.6×10^6 litre mole^{-1} s^{-1}, the corresponding values for γ-tocopherol and δ-tocopherol being 1.3×10^6 and 0.5×10^6 litre mole^{-1} s^{-1} respectively[29,30]. These values exceed by 1–2 orders of magnitude the rate constants for the reactions with radicals of a number of familiar synthetic inhibitors investigated using the same model[31]. One of the interesting characteristics of tocopherols as antioxidants is a high stoichiometric coefficient of inhibition, which is 4.5 for α-tocopherol and 3.5 for γ-tocopherol[10,32]. This large number of chains terminated by one inhibitor molecule can be explained according to the authors by the inhibiting activity of the product formed from tocopherol when it interacts with free radicals. According to Tappel's mechanism, the phenoxy-radical derived from tocopherol is converted into a benzyl radical, reducing at the same time the OH group[33]. As a result of these rearrangements, one α-tocopherol molecule can react with six peroxy-radicals and one γ-tocopherol can react with four peroxy-radicals[32]. Despite their high antiradical activity, tocopherols are weak antioxidants. Thus the inhibition of the oxidation of methyl oleate and arachiden by α-tocopherol is six and three times less effective than the inhibition by the familiar inhibitor 2,6-di-t-butyl-4-methylphenol (ionol)[34,35]. It has been suggested that this is due to the high activity of the radicals formed from tocopherol, which can enter into the chain-propagation reaction and thereby weaken the effect of tocopherol as an inhibitor[36-38].

The contribution of tocopherol to the overall antioxidant activity of mouse liver lipids does not exceed 15–20% and its contribution to the antiradical activity does not exceed 40–60%.[34]

Many investigators attribute a high antiradical activity to ubiquinones, among which coenzyme Q_{10} is the most active[39,40]. The mechanism of their antiradical action is obscure. It is suggested that the ubichromenol form may be active[41]. Like tocopherols, ubiquinones are weak antioxidants[42–46]. Their relative antioxidant effectiveness is smaller by an order of magnitude than that of ionol and by a factor of 2–3 than that of tocopherol[40]. The reduced enolic forms of ubiquinones are comparable to α-tocopherol as regards their antioxidant properties[44,45]. This is because the enolic forms of ubiquinones have higher constants k_7. In our laboratory Khrapova and coworkers are making a comparative study of the antiradical effectiveness of the enolic and quinone forms of natural antioxidants. The greatest difference between the constants k_7 for these forms occurs for tocopherol, which is present in the organism mainly in the phenolic form (see Table).

The rate constants (litre mole^{-1} s^{-1}) for the interaction of the enolic and quinone forms of antioxidants with free radicals.

Antioxidant	Enolic form	Quinone form
Tocopherol	$2.6 \cdot 10^6$	$1.7\ 10^3$
Ubiquinone	$2.1 \cdot 10^5$	$5 \cdot 10^3$
Vitamin K	$3.9 \cdot 10^6$	$5 \cdot 10^3$

The ratio of the rate constants for different forms of vitamin K, which is present in lipids mainly as the quinone, is also fairly large. For ubiquinone, the difference between the rate constants is smaller, which demonstrates the ease of its transition from the oxidised to the reduced form and conversely (see Table). The contribution of ubiquinone to the antioxidant properties of liver lipids does not exceed 5–10%.[40]

Much attention has been devoted to the study of hormones as antioxidants. Thyroid hormones have been shown to exhibit antioxidant activity in the model reaction involving the oxidation of methyl oleate[46]. Amongst steroid hormones, the antiradical effectiveness of which has been studied on the basis of the quenching of chemiluminescence[47], oestrogens proved to be the most active. For example, in the model reaction involving induced oxidation of lipids in mitochondria, diethylstilboestrol has a constant k_7 of the same order of magnitude as tocopherol[47]. Adrenaline exhibits weak antiradical properties[38,48]. The antiradical action of hormones is probably associated with the presence of phenolic groups in their molecules.

There are many obscure aspects of the problem of the antioxidant action of phospholipids and its mechanism. Some studies demonstrated antiradical activity in certain phospholipids, for example in phosphatidylcholine[48], while in others it is asserted that the antioxidant activity of phospholipids can be manifested only in those cases where they are mixed with antioxidants, since phospholipids behave as synergistic agents for antioxidants[49,50]. Olcott and coworkers[51] suggested that the only phospholipids with antioxidant activity are those capable of being oxidised under the experimental conditions with formation of a nitroxy-radical, which exhibits antiradical properties.

The problem of the antioxidant activity of cholesterol is widely discussed in the literature. Cholesterol was found to have a weak influence on chemiluminescence in model systems[48,52]. However, it has not been established whether the quenching of the chemiluminescence by cholesterol is chemical or physical. The cholesterol concentrations at which an effect is observed are fairly large (0.01 M), which makes it necessary to treat with much caution conclusions concerning the antiradical properties of cholesterol. The behaviour of cholesterol in model lipid oxidation systems is fairly complex. The experimental result depends on the cholesterol concentration, the rate of oxidation of the model lipid, and the duration of oxidation. Thus it has been shown[53] that, in the oxidation of methyl oleate, cholesterol exhibits antioxidant properties in the range of moderate concentrations, while lower and higher experimental concentrations actually accelerate oxidation. The antioxidant activity increases with time. These findings can be accounted for if cholesterol is regarded as the substrate of joint oxidation with methyl oleate and when account is taken of the fact that the cholesterol oxidation products may be antioxidants. Indeed it was shown that cholesterol is oxidised via a free-radical mechanism[54] and that its oxidation can be retarded by radical-reaction inhibitors[55].

Thus the main lipid components of membranes—phospholipids and cholesterol—can play a decisive role in the changes of the overall antioxidant activity in lipids, but the mechanism of this influence is complex and at present has not been finally elucidated.

Summarising the foregoing, the following points may be noted:

1. Many substances present in the lipid phase of cells exhibit antioxidant and antiradical properties. The characteristic features of most of them are a relatively low antioxidant effectiveness.
2. The overall antioxidant activity of the lipid fraction is determined by the interaction of its components. The contributions of individual antioxidants to the antioxidant activity of lipids are comparable.
3. Although the antiradical properties of natural antioxidants vary within wide limits, this does not have a significant influence on their antioxidant properties, probably because of the high activity of the radicals derived from the inhibitor, which enter into the chain-propagation reaction and weaken the antioxidant properties of the inhibitor.

It has now been shown that endogenic antioxidants inhibit the lipid oxidation processes *in vivo* and fulfill their antioxidant function together with their other specific functions. In order to establish the role of natural antioxidants in cell metabolism, it is extremely important to elucidate the question of their interaction and capacity for interchange. It is known that many diseases entail a simultaneous decrease of the amounts of various antioxidants. For example a decrease of the concentration of not only tocopherol but also ubiquinones has been observed in vitamin E deficiency[56].

The changes in the amount of natural antioxidants in liver lipids following the introduction of tocopherol into animals have been studied[57,58]. Together with an increase of the steady-state concentration of tocopherol in lipids, there is a significant accumulation also of other natural antioxidants. According to the authors, this is a consequence of the preferential consumption of the added tocopherol in free-radical oxidation reactions, which is confirmed by an

increase of the concentration of tocopherylquinone—one of the final reaction products of tocopherols in these processes[58,59]. Similar results were obtained also in experiments where ubiquinone had been introduced[40]. These results indicate indirectly the importance of the antioxidant properties of tocopherols and ubiquinones, on the one hand, and the absence of specificity in the inhibition of the free-radical oxidation of lipid, on the other.

In certain cases the deficiency of natural antioxidants can be made good by synthetic inhibitors. Thus certain synthetic antioxidants eliminate many symptoms of vitamin E deficiency, while others are inactive[60-63]. In order to establish the principle if the selection of synthetic inhibitors to make good the deficiency of the organism's own antioxidants, it is necessary to compare their effects.

The influence of the introduction of various inhibitors on the system of natural antioxidants has been studied[64,65]. It has been established that only inhibitors with antiradical activity k_7c (c is the inhibitor concentration in lipids) comparable to that of natural antioxidants are capable of replacing them in the free-radical oxidation of lipids and of increasing the steady-state concentration of natural antioxidants. Thus the introduction of propyl gallate increases the concentration of tocopherol in mouse liver lipids by a factor of 1.5, the concentration of tocopherylquinone decreasing. This supports the hypothesis that the rate of utilisation of tocopherol decreases owing to the competitive inhibition of the free-radical oxidation of lipids by the synthetic inhibitor. The overall antioxidant activity of lipids increases following the introduction of synthetic inhibitors both due to the presence of the synthetic inhibitor in lipids and, when preparations with high values of k_7c are introduced, as a result of the increase of the concentration of natural antioxidants.

Thus the influence of synthetic inhibitors on the amount of natural antioxidants in lipids can be accounted for on the basis of the usual competitive relations for two or several inhibitors. However, in experiments with the introduction of synthetic inhibitors into animals, phenomena were also observed, which cannot be simulated experimentally. Thus it has been found that, following the introduction of large amounts of synthetic inhibitors, AOA of lipids in animal organs initially increases to a maximum and then falls significantly below the normal values[66,67]. It has been suggested that synthetic inhibitors, which have many properties in common with natural antioxidants, suppressed their synthesis or enhance the reactions in which they are consumed[66]. The dependence of the degree of reduction of the level of lipid AOA by synthetic inhibitors on their ability to inhibit oxidation reactions has been investigated[65]. It was found that the reduction is greater the higher the relative antioxidant effectiveness of the inhibitor. When 2,6-di-t-butyl-4-methylphenol is introduced into animals in a dose of 100 mg kg^{-1}, the concentration of tocopherol in lipids falls[65] and tocopherylquinone accumulates at the same time[58]. The results of these studies suggested a relation between the ability of the synthetic inhibitors present in lipids to inhibit oxidation reactions and the rate of consumption of the antioxidants.

In order to determine the cause of the change in the consumption of antioxidants, the rate of generation of free radicals in lipids was studied by a chemiluminescence method[58]. When AOA of lipids is altered by the introduction of synthetic inhibitors, a related change in the capacity of lipids for oxidation is observed. Lipids exhibit a greater ability to form radicals the higher their antioxidant activity. In other words, with increase of the amount of antioxidants, the composition of lipids changes in such a way that the rate of generation of free radicals from them increases with a corresponding increase in the rate of consumption of antioxidants[69]. Thus, after the introduction of tocopherol into animals, AOA increases by a factor of two and the capacity of their lipids for oxidation increases by a factor of about ten. Similar data were obtained after the introduction of propyl gallate and 2,6-di-t-butyl-4-methylphenol as well as in other processes associated with a change in the level of AOA of lipids. It is noteworthy that the relation between AOA of lipids and their capacity for oxidation on the one hand and the corresponding rate of consumption of antioxidants on the other is satisfactorily linear[64].

The existence of this relation ensures the maintenance of a constant level of oxidation reactions in lipids regardless of whether their AOA has changed as a result of the change in the amount and quality of the natural antioxidants or as a result of the presence of synthetic inhibitors. The product k_7c determines which antioxidants, endogenous or those introduced into the organism, will be the first to be consumed and hence whether or not AOA of lipids will fall below the normal value.

Thus synthetic inhibitors of radical processes can be used to induce specific changes in AOA of lipids and probably to influence the course of diseases where a change in AOA of lipids is a significant factor.

III. THE INFLUENCE OF SYNTHETIC INHIBITORS ON PATHOLOGICAL PROCESSES INVOLVING CHANGES IN THE LEVEL OF ANTIOXIDANTS

It has now been shown that, in the development of a wide variety of pathological states, there is a change in AOA of the lipids in the organs and tissues[10,70].

In terms of the change in AOA of lipids, all the pathological states investigated and the changes in cell metabolic processes under the influence of particular environmental factors may be divided into three groups. In the first group radiation damage caused by radiation or by the introduction of radiomimetics[66,69,71-76], the state of stress caused by low temperatures[10,77,78], hyperoxia[79], hyperthermia[80], electrostimulation[81], poisoning with benzene[78], the ageing process[77,82], ischemia[83], etc. may be included among processes occurring at a reduced AOA level. It is important to note that the higher the rate of development of the given pathological state and the greater the involvment of a particular organ, the more marked is the decrease of AOA.

The changes in AOA of the lipids in the organs of tumour-bearing animals[66,68,84-90] and reparative regeneration processes in organs and tissues[91] belong to the second group of processes occurring mainly at an increased level of AOA. As in the first case, there is a relation between the rate of development of the process, the severity of the disease, and the change in AOA[90].

Processes which lead to a change in AOA by stages, for example the induction of malignant tumours (carcinogenesis)[92-94] may be included in the third group †. In the first stage of carcinogenesis, during a period equal to one-third

† Although in the first and second groups there are various stages in the changes of AOA, they continue over a very short time interval compared with the time required for the development of the process, so that one may assume that the processes occur mainly at an increased or reduced level of AOA.

of the time required for the induction of tumours, AOA falls. It increases subsequently, but normal values are reached only after a time interval approximately equal to one-half of the induction period. Finally, the third period is characterised by a sharp increase of AOA. The changes in AOA characteristic of different types of carcinogenesis are of a general type and the curves describing them can be combined into a single general curve[92].

The most interesting and important finding is that a wide variety of pharmacological agents (vitamins, hormones, adaptogens, alkylating preparations, antimetabolites, cytostatic agents, aliphatic acid esters, alkylindolinylamines, supermutagens, etc) influence AOA in doses sufficient for a manifest pharmacological effect. There are preparations which only increase AOA (for example hydroxypyridines), those which only decrease AOA (alkylating agents), and those which can both increase and decrease AOA (adaptogens, radical reaction inhibitors, hormones, antimetabolites, derivatives of nitrosoalkylurea, etc.)[65,71,86,87,90,95-99].

The possibility of using these compounds in the treatment of particular diseases is associated with the nature of the influence of the preparations on AOA. If the pathological process takes place at a reduced AOA level, a wide variety of compounds which increase antioxidant activity have a protective effect, which is more marked the greater the increase of AOA which they induce[69]. On the other hand, preparations which diminish AOA are effective in processes occurring at an enhanced AOA level[71,89,90,95]. For example, all antitumour preparations decrease AOA and the degree of inhibition of tumour growth is greater the more marked and longer lasting is the decrease of AOA by these substances[89,90].

The relation between the influence of the preparation on AOA and on the course of a particular pathological process was demonstrated most strikingly in a study of preparations which can both increase and decrease AOA (depending on the dose) or when the same preparation is introduced at different times during the development of the process occurring with changes in AOA by stages.

As stated above, the introduction inhibitors in small doses increases the antioxidant activity of lipids with subsequent recovery to the normal value, while large doses lead to an increase of AOA and its subsequent fall below normal values. The characteristics of the action of synthetic inhibitors used in the treatment of a wide variety of pathological states of the organism are associated with these properties. Thus it has been established that the ability of the inhibitor to protect against radiation increases with its dose, reaching a maximum for the optimal dose (C_{opt}), and then decreasing. At a certain negative inhibitor dose (C_{neg}) no effect is observed and with subsequent increase of the amount of antioxidant there is a transition from protective to sensitising properties of the inhibitors[74,100-102]. A similar effect is observed when the inhibitors are introduced both before and after irradiation[103]. C_{opt} is the maximum amount of the preparation for which AOA of lipids does not decrease below the normal value[66,74].

A similar dual effect on tumour growth has been observed: small doses of the inhibitor accelerate and large doses retard the development of the tumour. The accelerating effect on tumour growth is observed in the range of doses below C_{opt},[86,89] while antitumour activity is observed for doses greater than C_{opt}.[66,68,88,89] Since the influence on tumour growth is more marked the greater the reduction of AOA by inhibitors, for each preparation there is an inverse relation between its antitumour properties and its ability to protect against radiation[104-106]. The antitumour effect of equimolar doses of preparations is greater the lower the value of C_{opt} for these inhibitors[104]. In the dose range from C_{opt} to C_{neg} inhibitors can be useful in the radiotherapy of tumours[106].

Data for the variation of AOA in tumour growth, on irradiation, and following the introduction of inhibitors led to the prediction and subsequent experimental confirmation[107-109] of the existence of four regions of different effects of the joint application of radical-process inhibitors and irradiation on the tumour and the organism of the tumour-bearing animal. In region I of inhibitor doses and irradiation the preparation protects both the animal and the tumour from the action of radiation. in region II the preparation enhances the action of radiation on both the organism and on the tumour, in region III the preparation protects the tumour but sensitises the organism to the action of radiation, and finally in region IV the preparation enhances the effect of radiation on the tumour and at the same time protects the organism[108].

The available literature data for the anticarcinogenic effect of antioxidants behaving at the same time as radical process inhibitors are extremely contradictory. It has been shown that both natural (vitamin E) and synthetic antioxidants can retard tumour growth[93,94,110-117], have no effect whatever[118-120], and can "promote" carcinogenesis[121-123].

Since in the tumour induction process there are stages involving a decrease and an increase of AOA, different effects can be expected following the introduction of inhibitors in different doses and at different stages of carcinogenesis. Indeed, the introduction of an inhibitor belonging to the class of screened phenols in a dose which only increases AOA led to the arrest of the formation of tumours in the initial period and to a decrease of the percentage of tumours formed. On the other hand, if the same amount of the preparation was introduced at the stage corresponding to the increase of AOA, the tumours appeared sooner. The reverse behaviour was observed when large doses of inhibitors, causing a decrease of AOA were introduced[124]. From these standpoints, the discrepancies in the literature data are not unexpected.

One of the important aspects of the use of inhibitors is their application to protect the organism under stress, in the course of which AOA decreases. Synthetic inhibitors applied in doses increasing AOA exhibit antistress activity and protect animals from hyperoxia[79], poisoning by benzene[78], and stress due to cold[77,78]. The introduction of inhibitors in doses decreasing AOA enhances the effect of the stress-inducing agent[78]. Numerous studies have been made on the protective properties of tocopherol in poisoning by carbon tetrachloride and in intoxication by ozone. These have been reviewed[125].

It has been shown[83] that in the experimental ischemia of kidneys lipid AOA decreases and inhibitors applied in doses increasing AOA exhibit anti-ischemic activity, significantly prolonging the life of the animal.

An important property of the inhibitors, which opens up new fields for their application (for example in tissue and organ transplants), is their ability to influence specifically the rate of cell multiplication. In small doses inhibitors accelerate cell multiplication both in reparative regeneration[91] and when introduced into intact animals, increasing the level of the proliferative activity of the cells of their organs[126]. In doses decreasing AOA inhibitors retard cell multiplication. In the light of these facts, the desirability of employing inhibitors as geroprotectors is evident[127].

Although not all the aspects of the application of radical-process inhibitors have been considered, the principal features of antioxidant therapy are already clear from the data presented:

1. Inhibitor-antioxidants can be used in the treatment of diseases involving a reduced level of AOA. The preparations are more effective the higher the level of AOA following their introduction.

2. Inhibitors can be used also to suppress processes involving an increase of AOA. The inhibiting effect is shown only for inhibitor doses which reduce AOA.

3. Depending on the dose and the method and duration of introduction, the effect of the inhibitor can be reversed. The contradictory data concerning the therapeutic effects of preparations of this class are probably associated with this fact.

4. There is a consistent relation between different aspects of the biological activity of antioxidants, and their effectiveness has been found to depend on their physicochemical constants as inhibitors. This suggests that antioxidant properties are the cause of the wide spectrum of the biological activity of radical-process inhibitors. Furthermore, this justifies an initial selection of antioxidants on the basis of physicochemical models and makes it possible to recommend the synthesis of inhibitors which are most effective in a particular application.

IV. THE ROLE OF ANTIOXIDANTS IN THE STRUCTURE AND FUNCTION OF MEMBRANES

The problem arises of the causes of the significant role of the changes in AOA in the development of the pathological process and of the basis of the therapeutic activity of preparations normalising AOA.

Lipids together with proteins are the most important components of membranes. If it is assumed that antioxidant properties are indeed important for the functioning of membranes, there should be a correlation between the changes in these properties in the membranes of various organelles and the changes in their function, depending on AOA.

Together with the study of the widely known regulatory mechanisms in the cell (such as the repression–derepression of genes, the blocking–deblocking of the genome, the inhibition and activation of enzymes by allosteric effectors, and regulation with the aid of a secondary hormone mediator–c-AMP, etc) much attention is devoted nowadays to the study of the role of membranes in the regulation of cell metabolism. Numerous instances of the experimental confirmation of the Konev–Changeux hypothesis concerning the important role of cooperative transitions in the membrane in the switching of cell metabolism occurred in recent years[128,129].

The receptor function of membranes, compartmentalisation, the contact of properties of cell surfaces, and the transport function of membranes are all aspects of their funtional activity which can be regarded as the most important regulatory mechanisms of the vital activity of the cell. The relation between the structure of membranes and their functions is well known. Structural organisation in its turn is closely related to the physicochemical properties of the main components—lipids and proteins. The presence of antioxidants in the lipid phase of the membranes has been regarded by a number of workers as an obligatory condition for the maintenance of the membrane structure, since the development of peroxide oxidation in lipids leads to its breakdown[130,131]. There exists the hypothesis that lipid antioxidants also play an intrinsic structural role in the membrane[132] The changes in AOA of the lipids in liver homogenate have been compared[133] with the changes in AOA of the lipids in various cell fractions. It was observed that both in the lipids from the nuclei and from the microsomes and mitochondria the nature of the changes in AOA is virtually the same as in the homogenate in all the instances investigated.

The fractions of AOA corresponding to lipids of particular organelles are various and change with time, which suggests a redistribution of AOA among the subcellular fractions. The instant of the attainment of AOA maximum is somewhat different for various fractions. Such data have been obtained in the normal physiological variation of AOA—the daily rhythm: after the introduction of a synthetic antioxidant, after the recovery of the weight of the liver following partial hepatectomy, under the influence of radiation, and in tumour growth. Thus the changes in AOA in the organelle lipids are of the same type, although they differ in scale and duration.

It is important to consider whether the change in the functional activity of membranes leads to a change in the antioxidant activity of their lipids. It has been established[134] that, when cells pass from stage G_1 to the stage of DNA synthesis, there is a sharp phased decrease of lipid AOA both in the nuclei and in the entire homogenate. Comparison of the change in the functional state of mitochondria and lipid AOA[133] also shows that an increase of AOA leads to an increase of respiratory control and a transition of the mitochondria to the most completely regulated state. For microsomal fractions, a change in functional activity was observed in processes involving a change in AOA[135].

Thus an increase or decrease of lipid AOA in the homogenate leads to consistent changes of the same type in lipid AOA in the organelle membranes and to corresponding polyfunctional rearrangements of their metabolism.

In discussing the mechanism of the influence of free-radical oxidation reactions in lipids on the functioning of membranes, the following versions may be considered[10]:

1. The appearance of polar peroxy-groups in lipids can lead to a change in the intensity of hydrophobic interactions and can influence lipid–protein bonds in the membrane.

2. The free valence in the lipid components of the membranes can alter the stability of the complexes of enzymes and other macromolecules, for example DNA, with the membrane. Therefore even a slight change in free-radical concentration can alter the cell metabolism.

3. The change in the rate of oxidation reactions in lipids is associated with the change in lipid composition. At the same time it is known that phospholipids are cofactors and effectors for enzymes and that a change in their relative content can have a significant influence on metabolism.

4. The functioning of the membrane leads to a change in its conformation or is accompanied by such a change. The structural transitions in membranes are in their turn induced by conformational and phase transitions in proteins or lipids. Therefore a change in the physicochemical properties of lipids can alter the physicochemical properties of the membranes and hence their functional activity.

As stated above, the present author observed that both at the cellular and membrane levels the lipid composition changes in response to an increase in AOA in such a way that the lipids are more easily oxidised. Since the oxidised forms of lipids are more popular, one could postulate that their formation is a method whereby lipids can leave the membrane and their composition can be restored[136,137]. Then an increase of AOA should retard the release of the most readily oxidisable lipids. This should result in an enrichment of the membrane lipids in these fractions, which should in turn accelerate the utilisation of antioxidants.

It has been established[53,138] that the increase of AOA induced by the introduction of synthetic antioxidants leads to an increase of the relative amount of phospholipids and to a decrease of the amount of cholesterol. Changes are also observed among the phospholipid fractions. With increase of AOA, the lipids in the liver cell membranes are enriched in phosphatidylserine, phosphatidylinositol, and phosphatidylethanolamine—the more readily oxidised fractions of phospholipids. A decrease of AOA leads also to a decrease of the relative amount of such fractions and to an enrichment of lipids in sphingomyelin and phosphatidylcholine[136,139]. Thus the changes in the rates of oxidation reactions in lipids and in their compositions are interrelated in a single system, which ensures the steady-state oxidation of lipids.

We shall consider further the results of the change in the relative composition of membrane phospholipids. As stated above, a change in the composition of membrane lipids leads to a change in their microviscosity and influences their structural rearrangements in membranes. This results in an intensification or a weakening of the metabolic activity of enzyme proteins incorporated in the membrane.

To elucidate the influence of AOA on membrane structure, a study was made of the change in the state of biomembrane components using spin probes located preferentially in the lipid or protein phases of the membrane[140]. The following iminoxy-radicals were used for the investigation: 4-capryloyloxy-2,2,6,6-tetramethylpiperidin-1-yloxy-radicals (probe I), and 2,2,6,6-tetramethyl-4,5-benzo-1,2,3,4-tetrahydrocarbolin-3-yloxy-radicals (probe II). Probe I was located preferentially in the lipid components of the membrane and probe II in the protein components. The influence of temperature on the mobility of the spin probes in the membranes of the organelles (nuclei and mitrochondria) in the cells of organs in intact animals and following the introduction of synthetic antioxidants was investigated. At 27° and 40°C there was a general conformational transition in the membranes, revealed with the aid of both probes. An increase in lipid AOA by the introduction of the antioxidant displaces the conformational transitions towards lower temperatures. It is interesting to note that the microviscosities in the membrane lipids and proteins vary in the opposite directions: the rotational mobility of the radical increases in lipids and decreases in proteins. An extremum is reached in the lipid phase 24 h sooner than in the protein phase. Thus the introduction of the antioxidant leads to the formation of a more "liquid" lipid component and to a more viscous protein component.

The change in the antioxidant properties of membrane lipids in tumour growth and under the influence of radiation[140] also altered the microviscosities of lipids and proteins and the conditions governing the structural rearrangements in the membrane. These findings can be accounted for by a change in the composition of the lipids in these processes, since it is known that a change in the cholesterol : phospholipids ratio and in the relative content of phospholipids alters the viscosity of the membrane components and the phase transition temperatures[141,142].

The second and no less important aspect is the influence of the change in the composition of lipids on the relative rates of the enzymatic reactions for which these lipids are effectors or cofactors.

It is known that the removal of phospholipids deactivates many enzymes and leads to the loss of their sensitivity to particular regulating agents[143,144]. The addition of phospholipids and cholesterol restores the activity of these enzymes and their sensitivity, the reactivating effect being frequently related specifically to the addition of a particular phospholipid. Thus β-hydroxybutyrate dehydrogenase is reactivated by phosphatidylcholine[145,146], adenylate cyclase by phosphatidylinositol[147], and FAD-dependent malate deydrogenase by cardiolipin[148]. The addition of phosphatidylserine to adenylate cyclase restores its sensitivity to glucagon[149] and the addition of phosphatidylinositol restores its sensitivity to noradrenaline[150]. It is extremely interesting that phospholipids behave as allosteric effectors for many regulating proteins[143]. This is not suprising, since the majority of the regulatory proteins have a quaternary structure enriched in non-polar aminoacids, for which hydrophobic interactions are extremely characteristic.

In view of the foregoing, it becomes understandable why a change in AOA leading to a change in lipid composition alters the structural viscosity of lipids, the lipid–protein linkages in the membrane, and the rate of the enzymatic reactions for which phospholipids are effectors. Owing to this, a change in the rates of oxidation reactions in lipids causes a transition of the cell to a new metabolic state characterised by new relations between the rate of particular enzymatic reactions.

The influence of lipids on regulating proteins permits an explanation of the possibility of switching the cell metabolism from one pathway to another when the composition of phospholipids is altered We may quote as an example the experiment in which a synthetic antioxidant was introduced into animals with a consequent increase of the concentration of phosphatidylethanolamine in liver microsomes together with an increase of AOA. According to model experiments[151], the addition of total phospholipids or of individual components reactivates or increases the activity of glucose-6-phosphates. It was of fundamental importance to establish the possiblity of regulating the activity of enzymes by lipids *in vivo*. In our laboratory Molochkina and Dzhalyabova observed that, simultaneously with the increase of the concentration of phosphatidylethanolamine, the activity of glucose-6-phosphatase increases in liver microsomes. A similar relation obtains not only following the introduction of antioxidants, but also in other processes accompanied by a change in AOA of lipids and hence in the concentration of phosphatidylethanolamine.

From the same standpoint, it is possible to explain also the role of lipids in the regulation of the rate of cell proliferation. As stated above, an increase of AOA leads to an increase of the concentration of phosphatidylserine and phosphatidylinositol, which function as effectors for adenylate cyclase. The influence of lipids on the activity and sensitivity of adenylate cyclase—the enzyme responsible for the formation of cAMP—makes it possible to explain the role of antioxidants in the regulation of cell proliferation at the molecular-biological level. Studies have been published recently in which much attention was devoted to the change in the composition of lipids during the synthesis of DNA. It is suggested that phospholipids form complexes with a DNA molecule, altering its stability, and are essential for the initiation of the synthesis of DNA[153,154]. Furthermore, *in vivo* experiments established the influence of phospholipids on the matrix activity of the gene and a difference between the amounts of phospholipids in repressed and derepressed genes[154]. It has been shown[155] that a change in AOA and composition of nuclear lipids is associated with a change in DNA synthesis. An increase in the amount of sphingomyelin in nuclear lipids against the background of a sharp decrease of AOA at the beginning of DNA synthesis is particularly significant.

The above experimental data show that the change in the antioxidant properties of lipids, caused both by a change in the amount of intrinsic natural antioxidants and by the

introduction of non-toxic synthetic inhibitor-antioxidants, alters significantly the cell metabolism. The importance of the change in the antioxidant properties is associated with the role of membranes in the regulation of cell metabolism, the functional activity of the membranes being altered when the physicochemical characteristics and the composition of the membrane components are changed.

In view of the foregoing factors, synthetic inhibitor-antioxidants can be usefully employed to act specifically on a wide variety of processes occurring with change in AOA of lipids.

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Physicochemical Mechanism of the Damage Sustained by Deoxyribonucleic Acid under the Influence of Various Agents

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Data obtained in studies on the damage suffered by DNA molecules under the influence of ionising ultraviolet, or ultrasonic radiation, and chemical mutagens are reviewed. The application of chemical kinetic and other physicochemical methods (ESR, chemiluminescence, spin labels, electron microscopy, etc.) to the study of the mechanism of the damage to DNA molecules acted upon in different ways is considered and mechanisms whereby chemical and structural changes occur in DNA are analysed. The hypothesis of the free-radical mechanism of the damage sustained by DNA under the influence of radiation and of the possible use of radical-reaction inhibitors as agents offering protection from radiation is discussed and evidence for its validity is presented.
The bibliography includes 181 references.

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I. INTRODUCTION

In 1957 Emanuel[9] suggested that physicochemical and chemical kinetic methods be used to investigate many pathological processes such as radiation sickness, tumour growth, ageing, and others[1-5]. These processes were studied at various levels of organisation—molecular[6,7], cellular[8-10], and at the level of the whole organism[11-14].

Studies at the molecular level included analysis of changes in important biomacromolecules such as proteins[15-17], nucleic acids[18-23], lipids[24-26], and enzymes[27-29], slight changes in the structure of which can lead to the breakdown of the normal vital processes in the cell. Much attention has been devoted to the analysis of the damage suffered by nucleic acids, particularly deoxyribonucleic acid (DNA)[30,31].

It is known that the change in the structure of DNA acted upon in different ways can easily lead to the breakdown of hereditary information, to a change in the synthesis of specific proteins, and in many instances to cell death. The use of physicochemical methods for quantitative investigation of the damage sustained by the DNA structure under the influence of various factors in model experiments yields data about the primary molecular "events" leading to damage to the macromolecule. This information is important for the solution of the general problem of nucleic acids, associated with the processes involved in their functioning in the cell (in particular for the understanding of the mechanism of the occurrence of mutations or of the death of the cell).

II. THE CHANGE IN THE PHYSICOCHEMICAL PROPERTIES OF DNA UNDER THE INFLUENCE OF IONISING RADIATION. THE MECHANISM OF THE PROTECTIVE ACTION OF RADICAL-REACTION INHIBITORS

Only the first steps have been taken so far in many attempts to elucidate the physicochemical nature of the processes occurring in the irradiated cell[32-34]. To determine the characteristics of the development of reactions leading to the death of the cell, it is important to discover which cell structures are damaged and in what sequence. Numerous radiobiological studies have shown that the nucleus is damaged by ionising radiation[35,36], cell division is affected[37], and chromosomal aberrations occur[38]. It has been shown that the replacement of thymine in DNA by its halogenated analogues intensifies the sensitivity of the cell to irradiation[39,40]. Analysis of reduction processes in the irradiated cell established a relation between the chemical changes in the DNA macromolecule and the observed radiation-induced effect[41]. These data showed that DNA is one of the principal targets for radiation.

The first studies on the radiation-induced damage to DNA following the application of high radiation doses led to the detection of both chemical changes in the macromolecule (the formation of peroxides, evolution of ammonia)[42,43] and of structural damage in DNA (a change in the viscosity of the irradiated solutions)[44]. Later investigations demonstrated that the action of ionising radiation on DNA may lead to the single and double breaks in the macromolecular chains[45-48], to a chemical modification

of the bases, and to cross-linking between the complementary DNA chains[49-51].

As new physical, biochemical, and physicochemical methods for the investigation of biomacromolecules were developed, it was possible to differentiate the action of different radiation doses on DNA, which must be taken into account in studies on the mechanism of the radiation-induced damage to the cell and the organism as a whole. Thus the employment of the method of spin labels[52] for the analysis of the damage in DNA revealed conformational changes in the macromolecules under the influence of low radiation doses (0.5–8 krad)[53]. The spin label correlation time τ_c (the average time necessary for the rotation of the stable radical by 45°) and the associated inverse variation of the radical rotation frequency ν were calculated from the ESR spectra of spin-labelled DNA. These values yield information about the kinetics of the changes in the microenvironment of the label during irradiation. The observed sharp decrease of τ_c with increasing dose indicates a change in the DNA structure near the site of addition of the label (Fig. 1).

Analysis of the lg τ_c–$1/T$ curves made it possible to determine the temperature of the structural transitions (T_{st}), which shifts on irradiation towards lower values. This indicates conformational changes in the macromolecule. It was established that the values of T_{st} for DNA isolated from various sources differ significantly. Thus T_{st} for DNA isolated from tumour cells is lower than for DNA isolated from normal cells[53,54]. The observed difference may be caused by the fact that in tumour cell DNA there are more defects in the secondary structure[55]. The validity of this hypothesis was demonstrated by analysing the defects in the secondary structure of DNA, isolated from normal and tumour cells, by the kinetic formaldehyde method[56]. The applicability of this method to the analysis of structural damage in DNA for low γ-radiation doses (up to 5 krad) has been demonstrated[57]. The authors observed a single structural defect for 2600 pairs of nucleotides.

The conformational changes in DNA at low doses were also detected by pulse polarography[58]. Some investigators point out the possibility of damage to DNA bases at low doses (2–10 krad)[59].

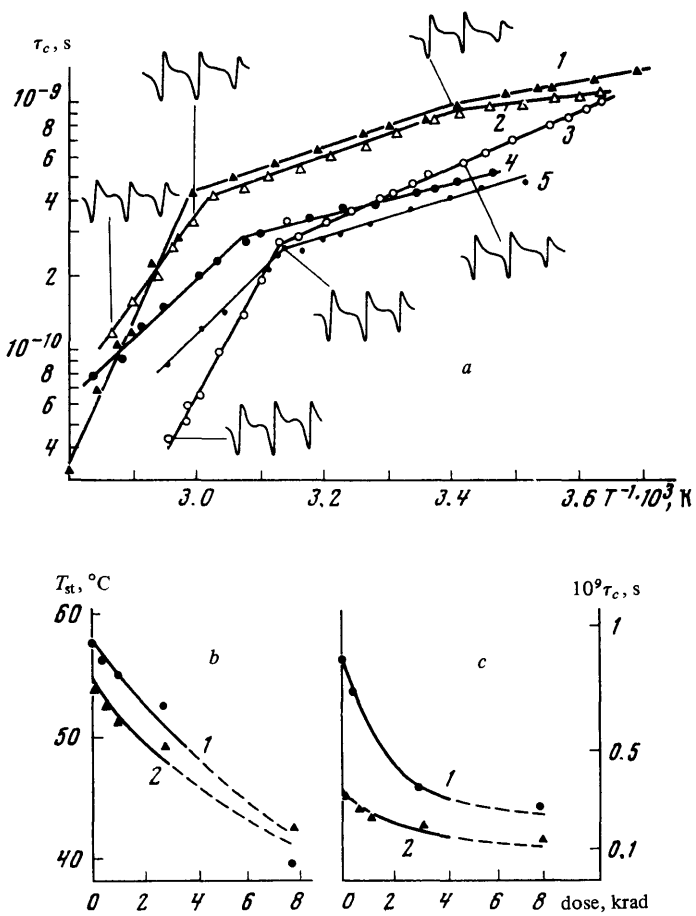


Figure 1. ESR spectra and temperature variation of the correlation time of spin-labelled DNA: *a*) [1) and 2) DNA isolated from the blood lymphocytes of two healthy cows; 3)–5) DNA isolated from the blood lymphocytes of three cows suffering from leukemia]; *b*) and *c*) variation with the dose of T_{st} and τ_c for DNA isolated from normal (curve *1*) and leukemic (curve *2*) cells.

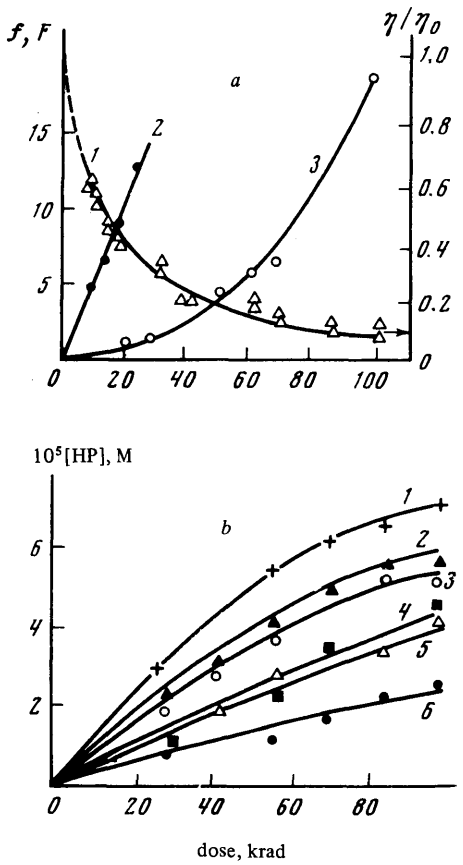


Figure 2. Variation of the physicochemical (*a*) and chemical (*b*) properties of DNA on irradiation with different doses: *a*) [1) intrinsic viscosity in relative units; 2) and 3) number of single (line *2*) and double (line *3*) breaks in DNA]; *b*) amount of DNA hydroperoxides formed on irradiation [DNA concentration (μg ml^{-1}): 1) 1000; 2) 700; 3) 500; 4) 400; 5) 100; 6) 50].

High doses (20–100 krad) lead to significant structural changes in the macromolecule (single and double breaks occur) and to chemical changes (the formation of hydroperoxides)[60–63] (Fig. 2). Infrared spectroscopy[64,65] made it possible to observe a modification of the bases at doses of 20–100 krad from the change in the intensity of the bands in the spectra of irradiated DNA solutions: deamination (3350, 3200, and 1600 cm^{-1} bands); saturation of double bonds (1580 and 1650 cm^{-1} bands); damage to the secondary DNA structure—rupture of hydrogen bonds (1700 cm^{-1} band) and of phosphate ester linkages (953 cm^{-1} band) (Fig. 3). The radiation-induced damage to DNA may be observed in electron micrographs of the macromolecule[66,67]. Long linear molecules are converted into short segments and coils after irradiation with doses in the range 60–300 krad.

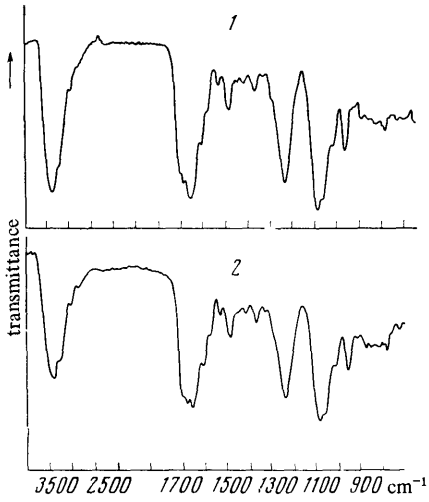


Figure 3. Infrared spectra of a calf thymus DNA film for 32% relative humidity: 1) native DNA; 2) γ-irradiated DNA (dose 55 krad).

The question arises of the causes of these significant changes in the DNA molecule and of the stages in the multistage mechanism of the damage sustained by the macromolecule where external action is necessary in order to liquidate or arrest the process. Several years ago Emanuel' put forward the following considerations on the basis of general concepts in chemical kinetics, radiation chemistry, and biochemistry[68]:

"1. The action of ionising radiation leads to the formation of free-radical states of the chemical components of the cell which may give rise to biochemical processes which are not characteristic of the living organism under normal conditions.

2. The development of free-radical reactions in the organism must lead to a decrease of the amount of inhibitors in the tissues, as happens in chemical radical processes induced by radiation in the presence of inhibitors. The decrease of the amount of tissue inhibitors impairs the ability of the organism to regulate correctly biochemical processes, which may be one of the causes of the changes characteristic of radiation sickness".

The above ideas made it necessary to investigate the free-radical states in biochemical systems, particularly in biomacromolecules—proteins, lipids, and nucleic acids. It has been shown by ESR[69,70] and chemiluminescence[71] methods that both the primary radicals formed in the course of irradiation of DNA and the secondary radicals generated as a result of the decomposition of hydroperoxy-compounds derived from DNA are important for the structural damage in the macromolecule.

The formation and reactions of DNA radicals were detected in the course of irradiation of aqueous DNA solutions at low temperatures (77 K). All the DNA radiolysis products are stable under these conditions[72]. It has been shown that the ESR spectrum of the irradiated DNA solutions contains lines due to paramagnetic species formed from water (ȮH radicals and stabilised electrons e_{st}) and DNA macroradicals. When the specimen is heated, the ȮH radicals and the electrons e_{st} vanish and the spectral lines due to the DNA radical appear. The doublet for the DNA radicals is gradually "converted" into a more complex quartet and at high temperatures (193 K) an eight-component spectrum is recorded, similar to that of the thymine radical[72,73].

With increase of DNA concentration in solution and of irradiation temperature, the yield of radicals rises. Kinetic curves for the accumulation of DNA radicals satisfy the equation $c = c_{st}(1-e^{-kD})$, where c_{st} is the steady-state concentration of radicals at high irradiation doses, k the rate constant for the destruction of radicals during irradiation, and D the radiation dose in Mrad.

To determine the nature of the radicals formed from DNA and the location of the free valence in the macromolecule, a study was made of the effect of radiation on compounds simulating individual fragments of the biopolymer—nitrogenous bases[74,75], carbohydrates[76–80], and phosphoric acid[81]. The formation of free radicals from nitrogenous bases was investigated under various conditions. The most detailed study was made of the formation and reactions of thymine radicals. It was established that thymine radicals are formed as a result of the interaction of an electron with a thymine molecule and the formation of a radical-anion, to which a hyperfine doublet structure corresponds in the ESR spectrum. On reacting with water, the radical-anion is converted into the thymine radical (of the type ṪH) (eight-component ESR spectrum). The observed hyperfine structure of the spectrum is due to the localisation of the unpaired electron at the $C_{(5)}$ atom of thymine[75].

The primary reaction in the formation of radicals in the sugar fragment of DNA is the abstraction of a hydrogen atom by ȮH radicals and free hydrogen atoms. Analysis of the ESR spectra of irradiated preparations of 2-deoxyribose and other carbohydrates[76,80,82] permitted an interpretation of the ESR spectrum of 2-deoxyribose as a result of the superposition of lines due to radicals in which the free valence is mainly located at the $C_{(1')}$, $C_{(3')}$, and $C_{(5')}$ atoms.

Irradiated frozen solutions of phosphate salts and phosphoric acid itself, DNA, and compounds simulating its sugar fragment were investigated by ESR. The ESR spectra of DNA did not contain lines characteristic of phosphoric acid radicals. This led to the conclusion that, even if the phosphate fragment in DNA is damaged, ultimately the free valence is located at the sugar fragment[81].

A comparative study of the ESR spectra of DNA, 2-deoxyribose, and nitrogenous bases led to the conclusion that at least two types of free radicals may be formed in DNA: with the free valence localised in the sugar fragment

and in the nitrogenous bases. The formation of radicals in DNA is possible as a result of both direct and indirect action of radiation.

The DNA macroradicals ($\dot{R}_{DNA}$) formed on irradiation are converted in the presence of oxygen into peroxy-radicals $R\dot{O}_2$ [72,73] and further into peroxide compounds (hydroperoxides):

$$\dot{R} + O_2 \rightarrow R\dot{O}_2 \rightarrow RO_2H.$$

Hydroperoxides are known to be radiotoxins and can in turn decompose with formation of radicals, initiating undesirable processes both in DNA solutions (a decrease of the molecular weight of the biopolymer, the occurrence of single breaks) and in the cell.

The formation of DNA hydroperoxides on irradiation has been established in a number of studies [84,85]. Kinetic analysis of the DNA hydroperoxide formation and decomposition processes showed [63,86,87] that hydroperoxides of two types are formed—relatively unstable and more stable. In a general form the rate constants for their decomposition can be represented as follows:

$$k_1 = 3.6 \cdot 10^5 \exp(-13000/RT),\ s^{-1};$$
$$k_2 = 1.3 \cdot 10^{11} \exp(-23000/RT),\ s^{-1}.$$

These expressions agree satisfactorily with the rate constants for the decomposition of hydroperoxides (HP) derived from thymine (k_t) and cytosine (k_c):

$$k_t = 4.5 \cdot 10^{11} \exp(-23000/RT),\ s^{-1};$$
$$k_u = 6.4 \cdot 10^5 \exp(-11500/RT),\ s^{-1}.$$

This suggested that, among the DNA hydroperoxides, those derived from cytosine and thymine are respectively less and more stable. The addition of inhibitors [88] demonstrated that the decomposition of cytosine hydroperoxide and hence of the less stable DNA hydroperoxide has a radical mechanism [87]. The decomposition of cytosine hydroperoxide (4.0×10^{-5} M) was retarded in the presence of α-naphthol, an effective inhibitor of free-radical reactions. The α-naphthol itself was consumed at a rate proportional to the rate of decomposition of the hydroperoxide, which indicated the possibility of the formation of radicals in the decomposition of cytosine hydroperoxide. In a study of the nature of the chemiluminescence of irradiated DNA solutions it was shown that the glow is due to the radical decomposition of DNA hydroperoxides and probably cytosine hydroperoxide [89-92]. This followed from a number of experimental findings (Fig. 4): a linear relation was observed between the chemiluminescence intensity and the concentration of hydroperoxides; the kinetic curve for the decomposition of the less stable DNA hydroperoxide had a shape closely similar to that of the kinetic luminescence curve; the activation energies for the chemiluminescence of the irradiated DNA solutions (E_{chl}) and for the decomposition of the less stable hydroperoxide (E_1) and cytosine hydroperoxide (E_c) had the following values:

$$E_{chl} = 13 \pm 1 \text{ kcal mole}^{-1};$$
$$E_1 = 13 \pm 1 \text{ kcal mole}^{-1};$$
$$E_c = 11 \pm 1 \text{ kcal mole}^{-1}.$$

The overall hydroperoxide decomposition mechanism can be represented as follows [22,71]:

$$ROOH \xrightarrow{k_0} R\dot{O} + \dot{O}H;$$
$$\dot{O}H + ROOH \xrightarrow{k_1} R\dot{O}_2 + H_2O;$$
$$R\dot{O} + R\dot{O} \xrightarrow{k_8} h\nu + \text{products};$$
$$R\dot{O} + R\dot{O}_2 \xrightarrow{k_{12}} h\nu + \text{products};$$
$$R\dot{O}_2 + R\dot{O}_2 \xrightarrow{k_{22}} h\nu + \text{products}.$$

Assuming a steady-state concentration of radicals in the system, it is possible to formulate equations for the rate of reaction of $\dot{O}H$, $R\dot{O}$ and $R\dot{O}_2$, the solution of which on the assumption that $k_8 = \sqrt{k_6 k_9}$ yields an expression for the concentration of these radicals. The destruction of $\dot{O}H$ radicals may be neglected since in the presence of ROOH the rate of their recombination is lower by several orders of magnitude than the rate of their reaction with ROOH. [93] The steady-state concentrations of the radicals are given by

$$[R\dot{O}] = \sqrt[6]{\frac{k_{22}}{k_6}}\,[R\dot{O}_2];$$
$$[R\dot{O}_2]^2 = \frac{k_0\,[ROOH]}{k_{22} + k_{12}\sqrt{k_{22}/k_6}}.$$

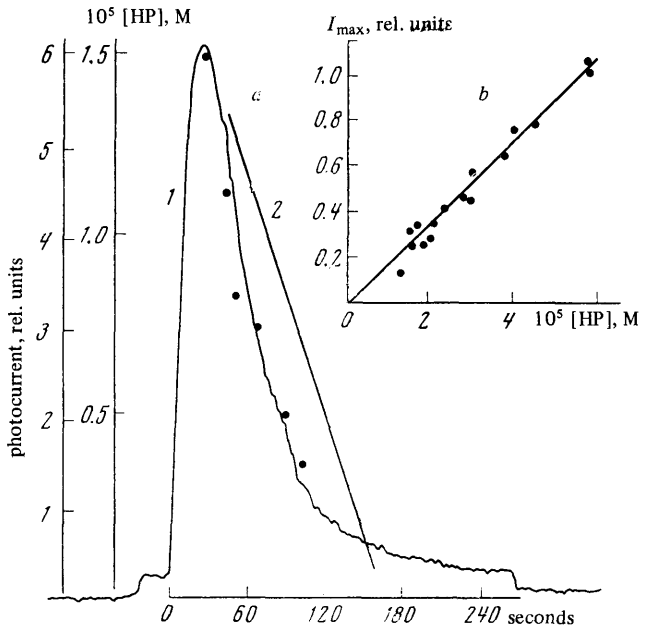


Figure 4. Chemiluminescence in the decomposition of DNA hydroperoxides: *a*) time variation of the chemiluminescence intensity (curve *1*) and of the concentration of the less stable hydroperoxide (circles on the curve) in irradiated DNA solution at 72°C; curve *2* is the semilogarithmic form of kinetic curve *1*; *b*) variation of the maximum intensity of the chemiluminescence of an irradiated DNA solution (700 μg ml^{-1}) with the initial concentration of hydroperoxides.

Since the chemiluminescence intensity I_{chl} is proportional to the rate of recombination of free radicals, one can write on the basis of the mechanism adopted

$$I_{chl} = Ak_6[R\dot{O}]^2 + Bk_{12}[R\dot{O}] \cdot [R\dot{O}_2] + Ck_{22}[R\dot{O}_2]^2.$$

Taking into account the expressions for $[R\dot{O}]$ and $[R\dot{O}_2]$, we obtain

$$I_{chl} = \alpha k_0\,[ROOH] = \alpha k_0\,[ROOH]_0 e^{-kt},$$

where

$$\alpha = \frac{Ak_{22} + Bk_{12}\sqrt{k_{22}/k_6} + Ck_{22}}{k_{22} + k_{12}\sqrt{k_{22}/k_6}}.$$

The expression obtained for I_{chl} agrees satisfactorily with experimental data [22].

Thus irradiation of aqueous DNA solutions may result in the formation of radicals both in the primary irradiation stages and as a result of the transformation of chemical products in secondary processes. Both reactions can be the primary cause of undesirable processes in the cell and can lead to breaks in the DNA chain and impairment of transcription. It was reasonable to suppose that the most effective means of preventing undesirable reactions involving free radicals might be inhibitors of free-radical processes (IRP), which have been used successfully in chemistry and have been proposed by Emanuel' [68] as agents offering protection from radiation (radioprotective agents or radioprotectors).

Studies on the radioprotective properties of IRP in model experiments with DNA [94,95] established that the most effective radioprotectors are derivatives of gallic acid, 3-hydroxypyridine, and phenylethylamine. The radioprotective effect of all the compounds under the conditions of appreciable damage to the molecule (60 krad) amounts to 80–90% when they are added before irradiation; derivatives of gallic acid and 3-hydroxypyridine exhibit a definite protective effect (20–48%) when they are used after irradiation [95]. Radical-reaction inhibitors greatly reduce the inactivation of the transforming activity of DNA under the influence of ionising radiation [96].

The observed linear relation between the protective effect and the antiradical effectiveness of the test compounds confirms the hypothesis of a significant role of free radicals in the damage to the DNA molecule and the analogous relation found in experiments on animals [97,98] shows that these compounds are promising radioprotective agents.

The protective effect of IRP added before irradiation can involve two mechanisms:

1. Via the interaction of the inhibitors with radical products of the radiolysis of water. This follows from the finding that the yield of DNA radicals on irradiation in the presence of propyl gallate (PG) is significantly reduced (G is 0.1 without PG and 0.02 with PG).

2. Via the reduction of the DNA radical by the inhibitor before the radical undergoes further reactions:

$$\dot{R}_{DNA} + InH \rightarrow RH + In\cdot.$$

This follows from experiments designed to study the changes in the DNA and propyl gallate radicals, irradiated at low temperatures, when the specimens are heated [99]. It has been shown that, when aqueous DNA solutions (5%) are irradiated in the presence of propyl gallate (0.03 M) at 77 K, $\dot{O}H$, $\dot{R}_{DNA}$, and $\dot{R}_{PG}$ radicals are formed. It has been established that, with increase of specimen temperature from 77 to 123 K, the $\dot{O}H$ radicals disappear, but the sum of the $\dot{R}_{DNA}$ and $\dot{R}_{PG}$ radicals remains unchanged. Subsequently, with increase in temperature from 173 to 193 K, the overall concentration of radicals does not alter, but $[\dot{R}_{DNA}]$ falls, while $[\dot{R}_{PG}]$ increases simultaneously. The operation of this mechanism of the protection of the macromolecule may be of interest in connection with the possible reduction reactions in the cell during irradiation.

As regards the protective action of inhibitors added after irradiation, presumably under these conditions they can interact with the radicals formed on decomposition of secondary products, for example hydroperoxides, and thus inhibit the reactions involving them. The intensity of the observed chemiluminescence of irradiated DNA solution decreased in the presence of various inhibitors (Fig. 5), the decrease being more marked the more efficient the inhibitor [90].

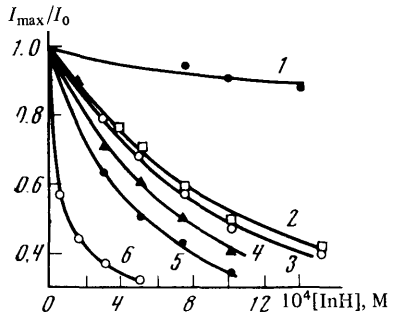


Figure 5. Variation of the intensity of the chemiluminescence of DNA solutions with the concentration of inhibitors at 72°C; inhibitor: 1) 4-ethylphenol; 2) hydroquinone; 3) catechol; 4) propyl gallate; 5) pyrogallol; 6) cysteine.

The mechanism of the possible reactions in this instance can be represented as follows [22,71]:

$$ROOH \xrightarrow{k_0} R\dot{O} + \dot{O}H;$$
$$R\dot{O} + InH \xrightarrow{k_7} ROH + In\cdot;$$
$$\dot{O}H + InH \xrightarrow{k_7} HOH + In\cdot;$$
$$R\dot{O} + R\dot{O} \xrightarrow{k_8} h\nu + \text{products};$$
$$\left.\begin{aligned} R\dot{O} + In\cdot &\xrightarrow{k_9} \\ In\cdot + In\cdot &\xrightarrow{k_9} \end{aligned}\right\} \text{without excitation of luminescence.}$$

This mechanism makes it possible to derive a relation between the intensity of the luminescence in the inhibited (I) and uninhibited (I_0) processes and the inhibitor concentration in the system:

$$\sqrt{\frac{I_0}{I}} = 1 + \frac{k_7}{\sqrt{2k_0k_8[ROOH]}}[InH].$$

A linear relation between $\sqrt{I_0/I}$ and the concentration of the inhibitor employed was indeed observed experimentally [91].

However, one should bear in mind that the reaction of the inhibitor involving the formation of free radicals may prove important in many cases as regards damage to cell components. Experiments on tumour cells by Lipchina, Pelevina, and coworkers [100] established that propyl gallate, the most effective radical-reaction inhibitor, can act in two ways depending on the experimental conditions. When PG was added to cells a short time before irradiation (15 min), a radioprotective effect was observed; on the other hand, when it was added to cells after 18 h, the latter were sensitised to radiation. The author suggested that the observed effect may be due to the possible damage of cell DNA by the PG reaction products.

To discover whether the PG reaction products can indeed react with the DNA molecule and how this affects the protective effect of PG, experiments were performed on isolated DNA where PG was added to irradiated DNA solutions at different times before irradiation and for

different degrees of oxidation of PG. [101,102] It was found that the addition of PG to the DNA solution immediately before irradiation results in a protective effect, which is enhanced with increasing PG concentration. The degree of protection falls when PG is added in an oxidised form or several hours before irradiation. The extent of the reduction of the protective effect increases with increasing contact time between PG and DNA before irradiation (Fig. 6).

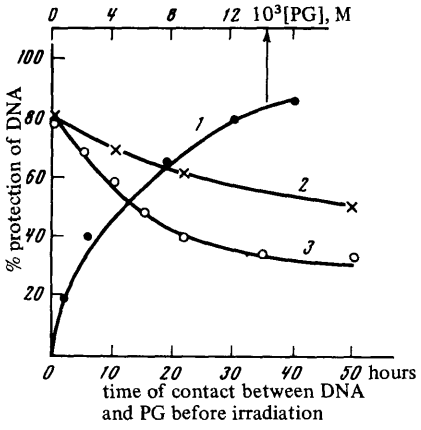


Figure 6. Effect of propyl gallate on the degradation of DNA during irradiation: 1) increase of the protective action in relation to DNA with increase of the initial propyl gallate concentration; 2) and 3) decrease of the protective action of propyl gallate in relation to DNA as a function of the duration of its contact with DNA before irradiation and of the degree of its oxidation [2) unoxidised propyl gallate; 3) propyl gallate oxidised to the extent of 30%].

One of the possible causes of the observed effect may be damage to the DNA structure by active PG oxidation products long before irradiation, which make the molecule more sensitive to subsequent irradiation.

Propyl gallate is known to be oxidised in an aqueous medium in the presence of oxygen, forming various biologically active radical and non-radical products: semiquinone radical-ions, quinones, etc. [103]. These intermediates can interact with the SH groups of proteins [104], can suppress the activity of many enzymes [105], can exhibit radiomimetic activity, and in particular can cause the rupture of chromosomes [106]. The formation of active radical intermediates is indicated by the chemiluminescence in the oxidation of PG. [102] The addition of DNA to the system both initially and at the instant corresponding to the maximum chemiluminescence intensity (Fig. 7) sharply reduces the yield of the oxidation products and the chemiluminescence. Free-radical oxidation products of the oxidation of PG were detected by ESR, their amount decreasing in the presence of DNA (Fig. 8). These findings show that the PG reaction products interact with DNA.

Experiments where PG oxidised to different extents had been added to DNA solutions showed that the longer the oxidation time of the added PG the more severe the damage to the DNA structure—single and double breaks appear in the molecule.

Thus, if one of the causes of the radiation-induced injury to cells is indeed damage of the DNA structure, then model experiments with isolated DNA will undoubtedly prove useful for the understanding of the mechanism of the damage of macromolecules and in the search for chemicals capable of causing specific changes in the sensitivity of the cells to radiation. In this sense radical reaction inhibitors are the most promising.

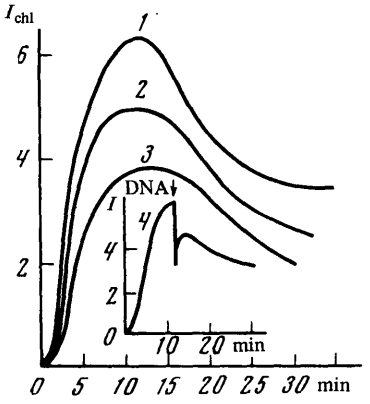


Figure 7. Variation of the intensity of chemiluminescence in the oxidation of propyl gallate: 1) at 70°C; 2) and 3) in the presence of added DNA at various concentrations [2) 80 μg ml^{-1}; 3) 160 μg ml^{-1}]; 4) variation of the chemiluminescence after the addition of DNA (80 μg ml^{-1}) at the instant corresponding to its maximum intensity.

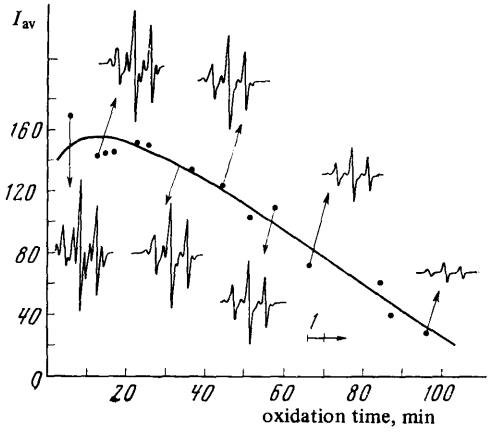


Figure 8. Variation of the intensity of the middle line in the ESR spectrum and of the shape of the propyl gallate spectra during oxidation in an aqueous alcoholic medium at 20°C and pH 11.5.

III. KINETICS OF THE DENATURATION OF DNA BY ULTRAVIOLET LIGHT

Ultraviolet light is known to be selectively absorbed by nucleic acids. DNA has been for many years the main object of studies on the effect of ultraviolet light at the

molecular level[107-109], since the nature of the observed changes in the cell[110] subjected to ultraviolet irradiation—mutations, chromosomal aberrations, and inhibition of cell respiration and DNA synthesis—indicate significant damage to the DNA.

The structural changes in DNA have been analysed by various physicochemical methods[111-116]. It has been shown that the exponential decrease of viscosity is associated with a parallel increase of optical density (hyperchromic effect), the kinetic constants for these processes having the same absolute magnitude (7.6×10^{-2} min^{-1}) [111]. Since it is well known that the hyperchromic effect is based on the impairment of the plane-parallel stacking of the bases due to hydrogen bonding and hydrophobic interaction between neighbouring bases are characteristic of native DNA, this agreement between the constants can be accounted for by the fact that the change in viscosity is due to the impairment of precisely these bonds. Thus the action of ultraviolet light reduces mainly to the denaturation of the molecule. This conclusion has been confirmed by the sedimentation analysis of DNA solutions after ultraviolet irradiation. It was shown that the sedimentation constant hardly changed in the course of the irradiation of DNA solutions (40 μg ml^{-1}) with ultraviolet light, which may indicate the absence of a sharp change in the molecular weight of the irradiated preparation[114].

The denaturation of the DNA molecule induced by ultraviolet light has been clearly illustrated by photomicrographs[112] recorded at specified time intervals. In the course of the first 5 min the photomicrographs show individual condensed sections which become clearly visible after irradiation for 20 min. On further irradiation (after 30 and 50 min) coils, the number and size of which increase, are visible in the field of view together with elongated molecules (Fig. 9). Evidently the denaturation process proceeds gradually with accumulation of denatured sections along the molecular chain.

These local conformational changes have been studied by ESR using 4-(β-aziridinopropionyloxy)-2,2,6,6-tetramethylpiperidin-1-yloxy-radicals as the spin labels[117]. It was shown that the denaturation of DNA is accompanied by an appreciable increase of the intensity of the ESR signal due to the label bound to DNA [115], which constitutes evidence that the label is joined in the first place to partly unwound or denatured sections of the DNA molecule.

The denaturation of the macromolecule can be followed by the change in the intensity of the signal of the label bound to DNA. Comparison of the changes in the ESR signal intensity I of the label and in the intrinsic viscosity of the solution η during the initial stage of irradiation showed that, as I increases η decreases. The change in the signal intensity of the label and the decrease of viscosity characterise to an equal extent the macroeffect of the ultraviolet irradiation on DNA solutions, i.e. the process in which local denaturation sites accumulate. The correlation times τ_c, which pass through an extremum (a maximum) as a function of the irradiation dose, were calculated. For low irradiation doses (up to 1.4×10^6 erg mm^{-2} for c_{DNA} = 600 μg ml^{-1}), τ_c increases, i.e. the mobility of the label diminishes; in the dose range ($1.4-3.5) \times 10^6$ erg mm^{-2} τ_c remains constant, falling sharply at still higher doses (Fig. 10).

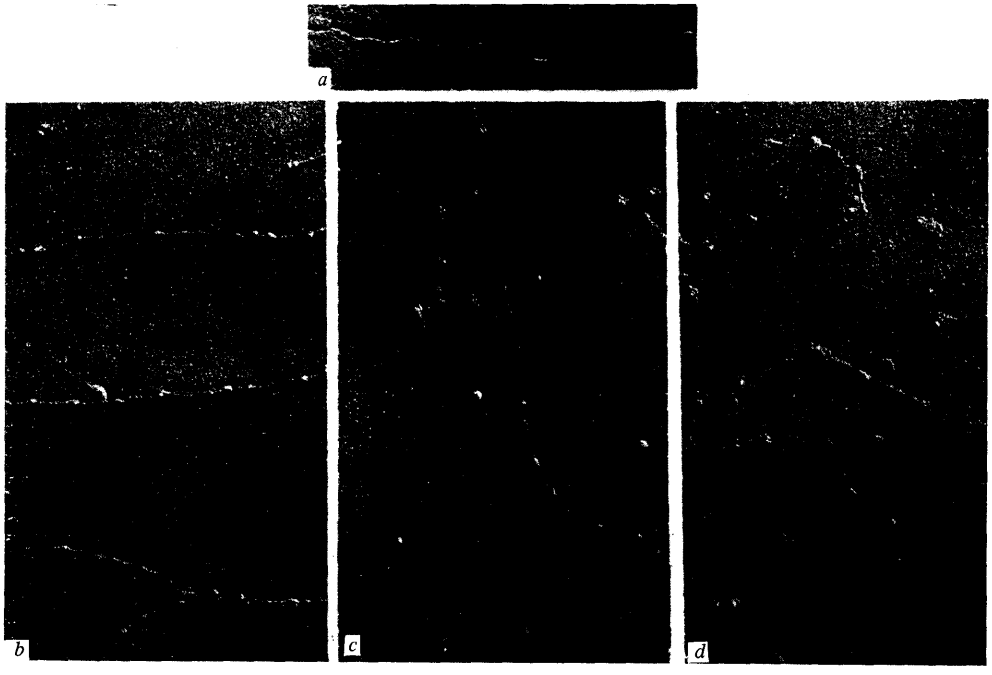


Figure 9. Photomicrographs of DNA preparations irradiated with ultraviolet light: *a*) fragment of the molecule of a native DNA; *b*) dose 3.6×10^5 erg mm^{-2}; *c*) dose 7.2×10^5 erg mm^{-2}; *d*) dose 1.2×10^6 erg mm^{-2}. The dimensions indicated in the photomicrographs correspond to 0.5 μm.

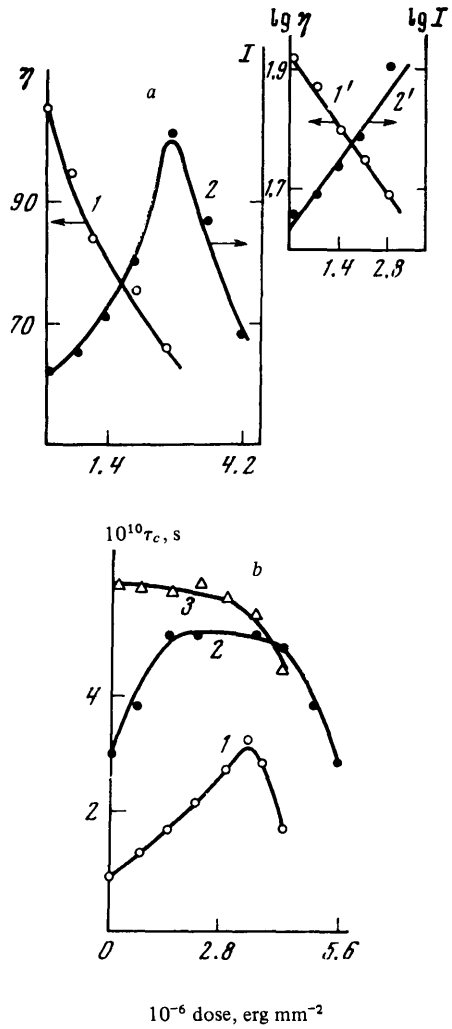


Figure 10. Variation of the viscosity and of the parameters of the ESR spectra of spin-labelled DNA as a function of the dose of ultraviolet irradiation: *a*) variation of the viscosity of DNA solutions (curve *1*) and of the intensity of the ESR signal (curve *2*) with the dose; lines *1'* and *2'* are semilogarithmic plots corresponding to curves *1* and *2*; *b*) variation with the dose of the correlation time for the spin label at different DNA concentrations [1) 400 μg ml^{-1}; 2) 600 μg ml^{-1}; 3) 900 μg ml^{-1}].

The decrease of the mobility of the radical may be caused by the increase of microviscosity within the local denaturation region. Two processes are known to occur in such regions: the accumulation of single breaks and the formation intramolecular cross-links as a result of the dimerisation of thymine bases. It has been suggested that thymine dimers accumulate in a single locally denatured region. The increase of τ_c can probably be a consequence of an increase in the yield of thymine dimers (for a single break in the polynucleotide chain). The constancy of τ_c observed in the dose range (1.4–3.5) × 10^6 erg mm^{-2} probably shows that the ratio of the thymine dimers and the breaks in the polynucleotide chain reaches a constant value. For fairly high doses (in excess of 3.5 × 10^6 erg mm^{-2}), the energy absorbed is consumed mainly in the formation of coils and globules. Under these conditions, the attached label is most probably distributed on the surface of the globule, which leads to a sharp increase of the mobility of the label and to a decrease of τ_c.

The structural changes in ultraviolet-irradiated DNA are indicated by infrared spectroscopic data. It has been observed[118] that ultraviolet irradiation of a DNA film with a 32% relative moisture content using a dose of 4.2 × 10^6 erg mm^{-2} decreases the absorption by the amino-groups of the bases by about 10%; the intensity of the C=N band at 1655 cm^{-1} falls by 10%, that of the C=C band at 1580 cm^{-1} falls by 25%, etc. The observed changes can be explained by the occurrence of photochemical reactions such as the dimerisation of thymine and the deamination of the cytosine dimer with its conversion into the uracil dimer[119]. The dimerisation reaction can be clearly followed in the infrared spectra of ultraviolet irradiated single-stranded DNA.[116]

A study of the denaturation of DNA by ultraviolet radiation led to the discovery of the phenomenon of the stepwise alteration of the rate constant for the decrease of viscosity as the concentration of the irradiated solution is altered[113]. It was suggested that the observed stepwise effect is due to the aggregation of DNA molecules in solution. The aggregation can be caused to some extent by the "cross-linking" of the macromolecules, including the dimerisation of thymine by ultraviolet light. Factors influencing aggregation (ionic strength, temperature) facilitated the manifestation of the "stepwise effect"; a decrease of ionic strength led to its complete disappearance. This is consistent with the data of Eigner and Doty[120] for the aggregation of molecules in solutions at different ionic strengths. The possibility of this behaviour follows also from the data of Doty and Glisin[121] concerning the dimerisation of the thymine in the DNA molecule in solutions at moderate ionic strengths and the decrease of the degree of dimerisation to a minimum at low ionic strengths. The stepwise effect was also shown in solutions at low ionic strengths to which metal salts (Ca^{2+} and Fe^{2+}), stabilising the DNA molecule, had been added.

Comparison of these results with data for the variation of τ_c of spin-labelled DNA solutions at different concentrations as a function of the irradiation dose shows that the minimum damage to DNA preparations occurs when the concentration is highest (900 μg ml^{-1}). This is probably a consequence of the maximum extent of aggregation of the macromolecules. Presumably the aggregation (it can also occur in a cage) "protects" the molecule from ultraviolet irradiation[115].

Since the changes in the DNA molecule observed under ultraviolet irradiation lead to a significant impairment of the vital processes in the cell, the question of seeking effective protective measures arises. Chemicals of various classes—phenols, pyrimidines, and mercapto-compounds—have been investigated[112] as protective agents. Propyl gallate, 3-pyridinol, hydroquinone, and thymine afforded 40–60% protection, while cysteine and glutathione afforded 15–17% protection. Estimation of the degree of absorption of ultraviolet light by the test compounds established that the main mechanism of the protective effect involves the screening of the DNA molecule. A similar protective mechanism was observed when glutathione, cysteine, and tryptophan were used in ultraviolet irradiation of cells[122].

The finding that the protective effect of radical-reaction inhibitors involves screening in such cases constitutes at the present time indirect evidence for the absence from

the system of appreciable concentrations of free-radical states. This is consistent with data obtained in studies[123,124], which demonstrated instantaneous recombination of the radicals formed on ultraviolet irradiation of aqueous DNA solutions at room temperature. The absence of stable radicals from ultraviolet irradiated DNA solutions was demonstrated by ESR[125]. The dominant role of the denaturation effects in DNA under the conditions of ultraviolet inactivation of bacteriophages has also been established[126].

Thus the use of physicochemical methods led to the discovery of structural and chemical changes in ultraviolet-irradiated DNA, which may be diminished by the introduction of various chemicals absorbing ultraviolet light.

IV. SPECIFIC FEATURES OF THE EFFECT OF ULTRASOUND ON DNA

Ultrasonic energy is used in making DNA preparations with various molecular weights for the investigation of the physicochemical and biological properties of DNA[127-130]. For this reason, the problem arises of the mechanisms of the depolymerisation of the DNA molecule and of the elucidation of the relative susceptibility to damage of its structural components.

It has been shown[131-133] that ultrasonic degradation of DNA, like that of other polymers, is mechanical. The existing ideas about the action of ultrasound on macromolecules indicate a dominant role of mechanical forces in the depolymerisation effect (shockwaves, hydrodynamic shear). The chemical changes in DNA are caused by the specific interactions of the molecule with activated dissociation products of water molecules (free radicals and ions) under cavitation condition[131]. Since the damage to the DNA structure by ultrasound can have consequences at the cellular level, the degradative changes in DNA were studied. The types of mechanical degradation of its strands and the initial chemical reactions of the carbohydrate–phosphate groups and the nitrogenous bases were investigated[134-136].

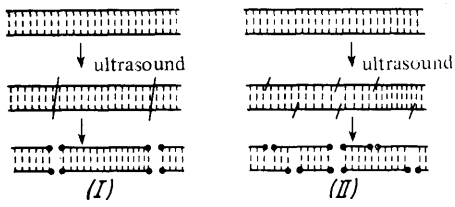


Figure 11. Schematic representation of various ways in which DNA is degraded by ultrasound.

Analysis of the physicochemical characteristics of single-stranded DNA[137,138] (sDNA) obtained from a native preparation (nDNA) subjected to ultrasound (UZG-250 generator, vibration frequency 750 kHz, intensity on the emitting surface 8–10 W cm^{-2}, duration of treatment 10–50 s) established that the DNA can be degraded either by the simultaneous rupture of both its strands (Fig. 11, scheme I) or by the independent accumulation of breaks in single strands (Fig. 9, scheme II)[131,136].

Ratios of the expected weight-average molecular weights of single-stranded DNA[139] and its intrinsic viscosities $[\eta]$ in 0.01 M Na^+ solution were calculated as a function of the postulated type of degradation of native NDA[135] from experimental values of F (the number of symmetrical breaks on depolymerisation of DNA) for s = 2 (where s is the maximum number of nucleotides between the breaks in the two DNA strands). The values of F were determined from the formula

$$F = \frac{M_0^{nDNA}}{M_t^{nDNA}} - 1 \quad .$$

The Table lists the experimental parameters of single-stranded DNA isolated from native DNA preparations exposed to ultrasound for given values of F and quantities calculated according to scheme I or scheme II. Evidently the experimental values agree with the calculated values for the degradation of DNA according to scheme I, i.e. as a result of the simultaneous rupture of both strands. There is no accumulation of random breaks in the DNA strands.

The molecular weights M and intrinsic viscosities of single-stranded DNA $\{[\eta]$ in 0.01 M $Na^+\}$ isolated from native DNA exposed to ultrasound and comparison with experiments of the values calculated in accordance with Schemes I and II.

Γ_{nDNA}	Scheme I		Scheme II		Experiment	
	$[\eta]$	$M\cdot10^{-6}$	$[\eta]$	$M\cdot10^{-6}$	$[\eta]$	$M\cdot10^{-6}$
0.28	57.3	2.29	5.6	0.22	58	2.32
0.45	53	2.12	4.46	0.18	52	2.08
0.77	46	1.85	3.48	0.14	46	1.6
2.03	31.6	1.27	2.2	0.09	23.5	0.94
3.75	22	0.88	1.6	0.06	13.7	0.55

Evidently DNA behaves as a single-stranded polymer in relation to the depolymerising action of ultrasound. The equation relating the rate of degradation of the polymer to the number of its strands is

$$\lg \frac{1-B}{B} = n \lg t + \text{const},$$

where

$$B = \frac{M_t^{nDNA}}{M_0^{nDNA}},$$

n is the number of strands in the polymer, and t the duration of action of the depolymerising factor. Fig. 12 shows that degradation by ultrasound does indeed obey the law characteristic of single-stranded polymers (with $n = 1$). Under these conditions, DNA having a molecular weight (M) of 1×10^7 is seen to decompose into fairly large molecules with M ranging from 0.3×10^6 to 1.2×10^6 (according to sedimentation analysis[129]). Ultrasound can thus be used to obtain native DNA fragments, which extends the scope of the application of ultrasound in biological experiments.

It is noteworthy that the observed depolymerisation of the macromolecules occurred under conditions of exposure to ultrasound where chemical processes associated with cavitation had not yet appeared. For longer exposures to ultrasound, leading to an increase of F, there is a slight discrepancy between the experimental data and the values calculated according to scheme I (see Table), which is probably due to the onset of chemoacoustic degradation of DNA. With increase of the duration of exposure to ultrasound from 1 to 15 min in the absence of protective substances, definite damage to individual chemical groups and bonds in the DNA molecule is observed. In particular, the intensities of a number of infrared absorption bands of DNA exposed to ultrasound change [136].

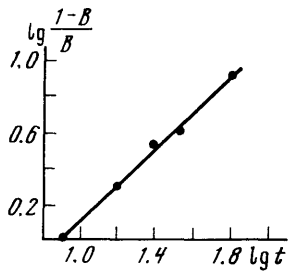


Figure 12. Kinetics of the depolymerisation of DNA by cavitation ultrasound.

In the region corresponding to the vibrations of the double bonds in the nitrogenous bases of DNA the intensity of the 1650 and 1590 cm^{-1} bands (due to the C=C and C=N bonds) diminishes, while in the region corresponding to the vibrations of the carbohydrate–phosphate chain the intensity of the 1010 cm^{-1} band [ν(COC) for deoxyribose] falls. Deoxyribose is then damaged to a greater extent than the nitrogenous bases: the decrease of the intensity of the 1010 cm^{-1} band is 17%, while that of the bands corresponding to the vibrations of the chromophoric groups of the nitrogenous bases is on average 10% (after exposure to ultrasound for 10 min). Deamination is observed only after more prolonged treatment with ultrasound.

The observed results show that the nature of the damage suffered by DNA on exposure to ultrasound differs from the effect of ionising radiation. As stated above, in the latter case the nitrogenous bases are deaminated together with the dissociation of their conjugated bonds; the bases are damaged to a greater extent. This difference is caused by the partial retention of the native DNA structure during ultrasonic degradation (caused by the simultaneous mechanical rupture of its two strands) and hence by the smaller accessibility to free radicals of the bases located within the helix. On the other hand, depolymerisation of DNA by ionising radiation entails independent accumulation of single breaks in each DNA strand [137,140], which must be accompanied by an appreciable damage to its secondary structure with a simultaneous damage to the rings of the bases.

In the literature on the infrared spectroscopy of DNA there is no unambiguous assignment of the 1060 and 960 cm^{-1} (970 cm^{-1} for a 92% relative humidity) bands to the vibrations of the individual C–O or P–O bonds of the carbohydrate–phosphate chains of DNA. A linear correlation has been observed between the relative decrease of the intensity of the 970 cm^{-1} band and the number of double breaks in DNA measured viscometrically. The correlation permits a tentative assignment of these bands to the vibrations of the C–O bond, since ultrasonic depolymerisation of DNA entails the preferential rupture of the C–O (90%) rather than P–O (10%) bonds [141]. The assignment of the 1060 cm^{-1} band to the vibrations of the C–O bonds appears to be less justified, since the intensity of this band does not decrease with increase of the duration of exposure to ultrasound.

A new band appears at 1190 cm^{-1} in the infrared spectra of DNA in the same wavenumber range. When DNA is ruptured, the number of terminal phosphate groups increases. The 1190 cm^{-1} band can be tentatively assigned to their vibrations, since absorption in the range 1190–1140 cm^{-1} is characteristic of alkyl phosphates. [64]

More far reaching changes in DNA under the influence of cavitation ultrasound led to successive decomposition of the pyrimidine and purine bases. Chromatographic analysis of the DNA hydrolysis mixtures exposed to ultrasound for periods ranging from 2 to 3.5 h demonstrated a greater resistance of the purine bases (adenine and guanine) to ultrasound compared with the pyrimidine bases (cytosine and thymine) [134]. This behaviour persists also in the susceptibility of the free bases and purine and pyrimidine derivatives to damage by ultrasound, which may have a definite biological significance.

The results obtained for the influence of ultrasound on the DNA molecule permit the employment of ultrasonic vibrations for specific and selective alterations in the DNA structure. The observed damage in DNA can have consequences at the cellular level, which has been confirmed, for example, by the formation on exposure of DNA to ultrasound of fragments with transforming activity [142] and by the results of studies on the influence of ultrasound on the chromosomal apparatus of cells and on genetic processes [143,144].

V. KINETICS AND MECHANISM OF THE REACTIONS OF AZIRIDINE DERIVATIVES AND NITROSOALKYLUREAS WITH DNA

More than 200 chemical mutagens have now been discovered. The great interest in compounds of this class is primarily due to the fact that chemical mutagens make it possible to obtain useful mutations in plants and microorganisms and have therefore found practical applications in the selection of agricultural crops and in the manufacture of antibiotics.

Since it has been shown that hereditary changes are mainly associated with nucleic acids (particularly with DNA), studies were begun to determine the possible mechanism of the action of chemical mutagens on DNA. A number of these established that mutations can arise both as a result of interaction with DNA (both in the state of replication and at rest) and as a result of reaction with its precursors. Under these conditions, alkylation of the bases and phosphate groups, replacement of one base by another, elimination of purines, etc. are possible.

The most effective mutagens proved to be substances with alkylating properties (derivatives of aziridine, *N*-nitroso-compounds, derivatives of mustard gas, epoxides, etc.). Studies *in vitro* and *in vivo* established a number of physicochemical characteristics of their action on nucleic acids. Some of the mutagens (aziridine derivatives,

mustard gas, etc.) cause changes in the macromolecule resembling the effect of radiation: a change in molecular weight, impairment of molecular shape, the formation of intramolecular and intermolecular "cross-links", etc.[145,146].

Since one of the principal problems in modern genetics concerns the possibility of achieving specific mutations, kinetic studies on the mechanism of the action of active mutagens assume particular importance. The effect of aziridine derivatives [2-aziridinylethyl methyl ketone (2-AEMK) and *N*-acetylaziridine (*N*-AA)] on DNA has been studied[147-152]. It has been shown that the effectiveness of these derivatives in terms of the intrinsic viscosity of DNA solutions increases in the sequence aziridine < 2-AEMK < *N*-AA.

The kinetics of the reaction and the physicochemical mechanism of the effect on DNA were studied in relation to *N*-AA. The kinetic curves for the variation of the viscosity of DNA solutions in the presence of *N*-AA are *S*-shaped and can be described by the equation for first-order autocatalytic reactions[151,147]:

$$\lg\frac{\eta_0-\eta_t}{\eta_t}=\lg\eta'+0.434\,\varphi t$$

$$\left(\text{when } \eta'\ll\eta_0,\ t>\frac{1}{0.434\,\varphi}\right),$$

where η_0 and η_t are the viscosities of the DNA solutions at the initial instant and at time t, lg η' characterises the size of the "seed" ensuring autocatalysis, and φ is the acceleration factor of the autocatalytic reaction. The changes in the kinetic curve show that the DNA molecule acted upon by *N*-AA undergoes not only conformational changes but also more far-reaching alterations with a change in the molecular weight.

The kinetic curve for the variation of the molecular weight of DNA can also be described in terms of the law governing first-order autocatalytic reactions, the value of φ being close to that for the variation of the intrinsic viscosity of the solution:

$\varphi = 0.31 \pm 0.02$ h^{-1} (from sedimentation data);
$\varphi = 0.28 \pm 0.02$ h^{-1} (from intrinsic viscosity data).

The changes in the DNA structure[147] discovered by electron microscopy are consistent with these observations. Only 2 h after the interaction of *N*-AA with DNA, the photomicrographs show modified DNA molecules (Fig. 13). The thickened regions formed throughout the extent of the molecule and at its ends lead to the conclusion that *N*-AA acting for a short period probably causes partial denaturation of DNA. At this instant the changes in the viscosity and molecular weight are very insignificant. After 12 h, low-molecular-weight fragments appear. By this time the molecular weight of DNA has fallen sharply. After 25 h, the photomicrographs show a large number of broken segments and coils resembling those observed after exposure to large radiation doses.

The action of 2-AEMK resembles that of *N*-AA. In this case too there is denaturation and depolymerisation of the molecules, but the reaction is slower.

The effect of aziridine (0.023 M) on DNA (1000 μg ml^{-1}) is somewhat different. After exposure to this substance for 2 min, thickened regions appear along the DNA molecule and at its ends, indicating partial denaturation. However, after 5 and 22 h the photomicrographs show, together with individual low-molecular-weight fragments, also large aggregates. A detailed study of the effect of brief exposure of DNA (50 μg ml^{-1}) to aziridine (10^{-4} M) was made using tungstophosphoric acid (TPA) as an electron-dense label which readily forms a salt-like linkage with the basic group of aziridine[150]. It was found that, after brief treatment with the mutagen (10 min), the density of the DNA filaments is uniform throughout the length of the molecule. Such uniformity of density is probably due to the fact that aziridine interacts with the phosphate groups of DNA. This is consistent with the literature data, showing that many alkylating agents can esterify the phosphate groups after acting on DNA for a short time.

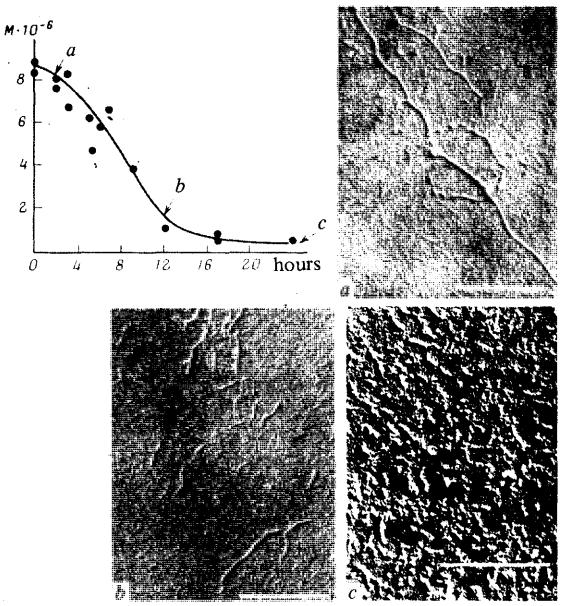


Figure 13. Photomicrographs of DNA and the kinetic curve for the variation of the molecular weight of DNA on interaction with *N*-AA; time (hours): *a*) 2.5; *b*) 12; *c*) 25.

A study of the effects of various concentrations of *N*-AA (0.012 M) on DNA[147] established that the change in the viscosity of DNA solutions remains autocatalytic in all cases. For the *N*-AA concentrations investigated, lg η' = 1.84 and $\varphi = 4.8\times10^{-2} - 2.3\times10^{-1}$ h^{-1}. The agreement of the values of lg η' for all the mutagen concentrations suggests that even at the initial instant the DNA–*N*-AA system contains the same amount of seed in all cases. Since the same DNA preparation was used in all the experiments, denatured DNA molecules, always present at the initial instant of the reaction, can evidently play the role of the seed. This is particularly likely, since denatured molecules are known to be more sensitive to various types of influences than the native molecules. The validity of this hypothesis was demonstrated in separate experiments using denatured DNA molecules[151].

DNA molecules denatured to different extents by ultraviolet light were added to the DNA-*N*-AA reaction mixture and the reaction rate was measured. It was shown that, with increase of the denaturation of DNA molecules, the induction period of the reaction fell, i.e. lg η' increased. Consequently the role of the denatured DNA molecules does indeed reduce to an increase of the amount of seed required to ensure the reaction between DNA and the mutagen.

Under the conditions of our experiments, the reaction of *N*-AA with DNA proceeds for a long time, in the course of which *N*-AA itself undergoes significant changes. It has been shown that the mutagen reaction products also play a definite role in the reaction. This is indicated by the "after effect" observed after removing the mutagen (Fig. 14). Thermochemical analysis of the transformation of *N*-AA made it possible to observe the conditions required for the formation of the maximum amount of the intermediate, the addition of which accelerated the process [149].

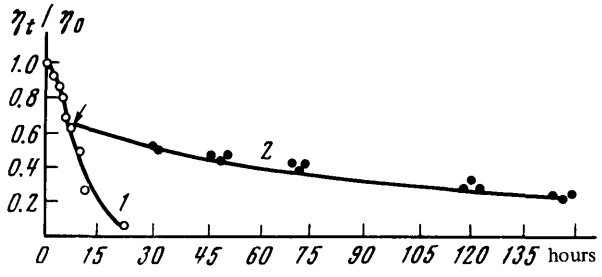


Figure 14. Variation of the intrinsic viscosity of DNA solutions acted upon by *N*-AA (curve *1*) and after the removal of *N*-AA (curve *2*) ("aftereffect"). The arrow indicates the time at which DNA was precipitated with alcohol.

The reaction of DNA with *N*-AA is accompanied by chemiluminescence [153], which appears 40 min after the start of the reaction and reaches a maximum in the course of 3 h with a subsequent slight decrease of intensity. The chemiluminescence spectrum consists of a broad band in the range 400–630 nm with a maximum at 490 nm. Kinetic chemiluminescence curves are *S*-shaped but are satisfactorily transformed into straight lines when lg $[I/(I_{max} - I)]$ is plotted. The chemiluminescence is due to oxidative processes, because its intensity falls sharply in the presence of O_2 and decreases in a stream of argon (Fig. 15). Since the change in the viscosity of DNA solutions containing the mutagen also occurs only in the presence of oxygen, the structural changes in DNA as well as chemiluminescence are probably a consequence of oxidative processes in the DNA–mutagen system.

In the reactions of the individual bases with *N*-AA there is no chemiluminescence, while in the reactions of nucleosides, nucleotides, and deoxyribose there is an appreciable chemiluminescence [154]. This shows that the reactions of 2-deoxy-D-ribose are responsible for the chemiluminescence. The latter probably arises as a result of the action of *N*-AA or its reaction products on the glycosidic carbon atom of ribose with subsequent oxidation at this atom. The stability of the glycosidic linkage is known to be influenced by the esterification of the hydroxy-groups and also by the nature of the base to which the carbon is bound: purine nucleotides are less stable than pyrimidine nucleotides and for this reason the chemiluminescence intensity in the reactions with purine nucleotides and nucleosides is higher than in the reactions with pyrimidine nucleotides. When deoxyribose is oxidised, the carbohydrate–phosphate linkages become labile and hydrolyse with rupture of the main macromolecular chain of DNA.

Radical-reaction inhibitors (propyl gallate, hydroquinone and 3-hydroxypyridine derivatives) reduce the chemiluminescence intensity to a greater extent the higher the antioxidant efficiency of the inhibitor [153].

Smotryaeva, Serebryanyi, and coworkers [155–158] investigated the mechanism of the reaction of DNA with *N*-alkyl-*N*-nitrosoureas (ANU). The interest in compounds of this class is not fortuitous, since, while behaving as supermutagens, they simultaneously exhibit both antitumour [159]

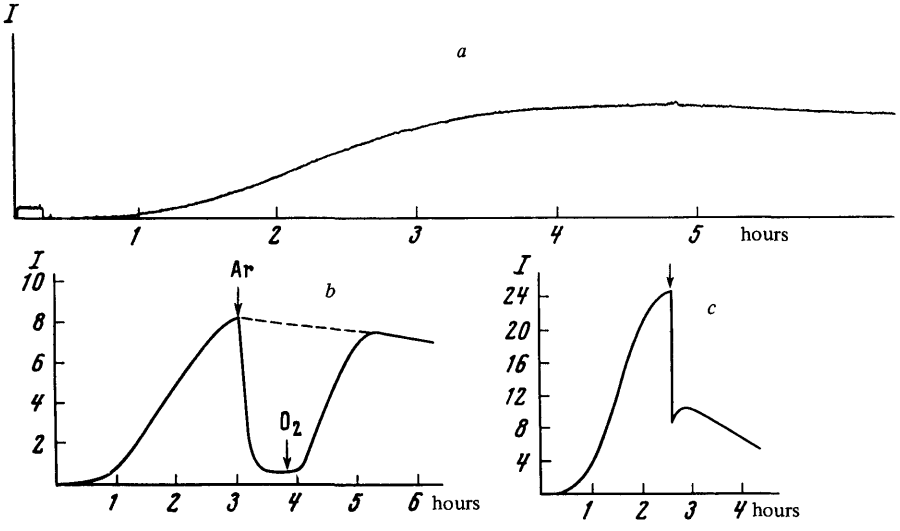


Figure 15. Chemiluminescence in the reaction of DNA with *N*-AA: *a*) kinetic chemiluminescence curve; *b*) variation of chemiluminescence intensity after the addition of argon and oxygen to the reaction mixture; *c*) variation of chemiluminescence intensity after the addition of propyl gallate at the instant corresponding to its maximum.

and carcinogenic[160] and mutagenic properties[161]. The reactions of *N*-alkyl-*N*-nitrosoureas with the genetic apparatus of the cell (in particular with the DNA molecule and the deoxynucleoprotein complex) can evidently play a significant role in such biochemical activity of the mutagens. One of the main physicochemical effects arising in the DNA structure as a result of its reaction with ANU is expressed by a sharp decrease of the viscosity of the solution and the occurrence of single and double breaks[156].

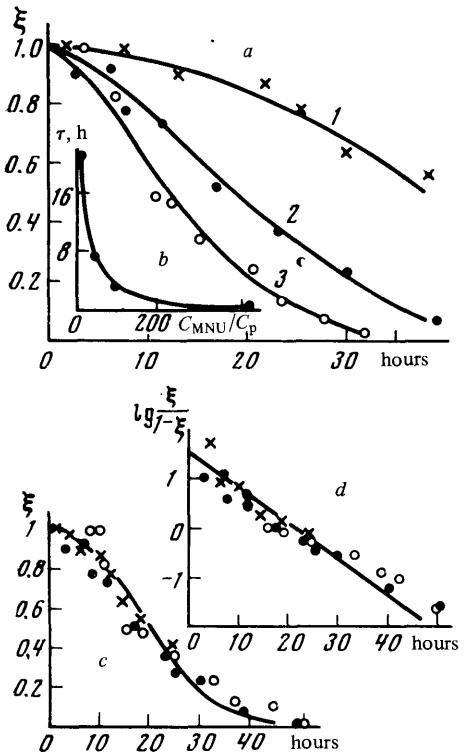


Figure 16. Kinetic curves for the variation of the intrinsic viscosities of DNA solutions (624 μg ml^{-1}) acted upon by MNU at different concentrations ($\xi = \eta_t/\eta_0$): *a*) [1) 0.02 M; 2) 0.1 M; 3) 0.2 M]; *b*) variation of the reaction induction period τ for different ratios of the amounts of MNU and DNA employed; *c*) transformation of the kinetic curves in *a* into curve *2*; *d*) semilogarithmic form of curve *c*.

The kinetic curves for the variation of the viscosity of DNA solutions in the course of reaction with *N*-methyl-*N*-nitrosourea (MNU) are *S*-shaped (Fig. 16), but give rise to straight lines when lg [$\xi/(1 - \xi)$] is plotted against time, in accordance with the equation for first-order autocatalytic reactions:

$$\lg\frac{\xi}{1-\xi} = \lg\xi' + 0.434\,kt,\quad t \neq 0,$$

where $\xi = \eta_t/\eta_0$ is a dimensionless coordinate characterising the viscosity of the DNA solution and lg ξ' and k are parameters of the kinetic curves. The kinetic curves for different concentrations can be transformed into a single curve with $k = 0.13$ h^{-1}.

The induction period of the reaction increases with decrease of the [MNU]:[DNA] ratio. In the course of the induction period chemical changes probably occur in DNA, which accumulate and are then manifested by single and double breaks in the DNA chains and by a decrease of the viscosity of the solutions (Fig. 17). This is also indicated by the experimentally observed aftereffect following the removal of the mutagen[155].

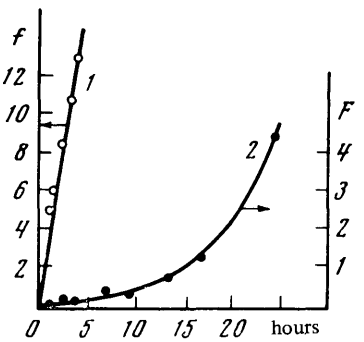


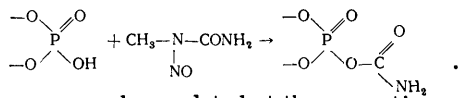
Figure 17. Damage to the DNA structure in the reaction with MNU: 1) accumulation of single breaks (*f*) in DNA molecules; 2) accumulation of double breaks (*F*).

A detailed study of the inactivating effect of MNU on different phages (T7, ΦX-174) showed that the reaction with DNA, in the first place alkylation of the DNA bases with subsequent elimination of purines from the alkylated fragments of DNA and degradation, may be responsible for the inactivation. A kinetic model has been proposed for the inactivation of phages, whereby it is possible to estimate quantitatively the influence of MNU on various phages[162].

More complex effects were observed in a study of the effect of MNU on deoxynucleoprotein[156]. It was shown that the strength of the DNA–protein linkage changes in the course of the reaction together with an integral property of the deoxynucleoprotein, namely its insolubility in a medium with the physiological ionic strength. The principal cause of the observed effect is chemical modification of the DNA and protein groups involved in the DNA–protein interaction and ensuring the integrity of the deoxynucleoprotein.

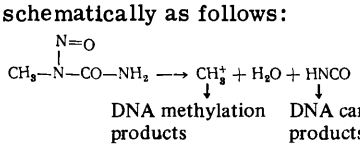
Analysis of the chemical changes in DNA and deoxynucleoprotein showed that the main chemical reaction giving rise to the degradation of DNA is again the alkylation reaction[157,163–165]. However, many biological data indicate a significant difference between the mechanism of the action of ANU and that of the action of other alkylating agents. To account for these differences, Serebryanyi[166] suggested that the ANU are agents with a complex action and their biological effect is due to the overall influence of two chemical reactions: methylation and carbamoylation. The use of MNU labelled with ^{14}CO in the reaction with DNA and deoxynucleoprotein established that there is indeed a transfer of the label from MNU to DNA and the protein, i.e. the carbamoylation reaction takes place[156,158]. The carbamoylation pathways were shown to occur in a study of the reaction of MNU with nucleotides, homopolynucleotides, and RNA.[167–169]. It was established that

mainly the phosphate groups are carbamoylated in polynucleotides:



The bases are carbamoylated at the same time, the main product of this reaction being N^4-carbamoylcytidine. Nucleotides can be arranged in the following sequence in terms of their reactivity in the carbamoylation reaction: cytidine ≫ adenosine ≃ guanosine, while in the alkylation reaction guanosine is the most reactive[168]. When MNU acts on the nucleotide complex, not only DNA but also the protein is methylated and carbamoylated[156]. The overall yields of both reactions are approximately the same; whereas both components of deoxynucleoprotein are methylated to an equal extent, mainly the protein is carbamoylated. Carbamoylation makes a significant contribution to the overall mutagenic activity of MNU, since carbamoylating agents such as isocyanic acid and its salts have been shown to possess mutagenic activity[170-172]. Later isocyanates were also found to have carcinolytic properties[173].

Thus the mechanism of action of MNU on DNA can be represented schematically as follows:



In connection with the antitumour properties of ANU, a study was made of the biochemical shifts arising after their administration *in vivo*. It was established that the synthesis of DNA, RNA, and protein is inhibited after the administration of ANU.[174-177]. The synthesis of DNA proved to be the most sensitive, that of RNA being inhibited to a lesser extent. In a study of the causes of the inhibition of RNA synthesis in a cell-free system it was shown that it involves both damage to the DNA matrix and a change in the properties of RNA polymerase due to the chemical modification of the enzyme. It is interesting that potassium cyanate, a product of the decomposition MNU, is also able to inactivate RNA polymerase[178].

The primary damage caused by MNU *in vivo* as well as *in vitro* arises as a result of methylation and carbamoylation reactions[179-181].

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Chemical Geroprotectors and the Problem of Increasing the Life Span

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The information available in the literature about the applications of geroprotectors—chemical substances used in experimental gerontology to increase the life span and to retard ageing—are described systematically and analysed. The proposed mechanisms of ageing are discussed only in connection with the characteristics of the action of the geroprotectors.
The bibliography includes 100 references.

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I. INTRODUCTION

Practical steps have been taken in modern gerontology in the search for agents which retard ageing.[1–3] Experimental gerontology endeavours to develop methods for influencing the ageing process whereby one could alter the biological limit of the life span, which cannot be influenced significantly by progress in medicine and by improvements in living conditions. The increase in life span by the retardation of growth and development, of the kind achieved in the experiments of McCay et al.[4] on rats, which were fed an inadequate diet, is evidently unsuitable for humans. This stimulated the search for other ways of prolonging life. The first hopeful experimental results of the employment of chemical substances to retard ageing were obtained at the end of the 1950s, the period when the theoretical development of this problem also began[5–8]. The chemicals and their mixtures used to increase the life span have come to be called geroprotectors.

On the initiative of Academician N. M. Emanuel', a combined study of the biological activity of radical-reaction inhibitors was begun in the 1950s at the Institute of Chemical Physics at the USSR Academy of Sciences. The hypothesis that free-radical processes are important in the development of certain pathological processes (radiation disease, malignant growth), in ageing, and in damage sustained by interaction with the environment proved to be fruitful. It promoted a successful search for biologically active substances, including geroprotectors, among anti-radical preparations.

No claim is made that the present review is exhaustive. Extensive data on the application of geroprotectors for the retardation of the ageing of cell cultures, the discussion of which would require the analysis of specific mechanisms of the ageing of the cell outside the organism, have been deliberately omitted. Those interested in this problem will find in this review references to original papers.

II. BIOLOGICAL ACTIVITY OF GEROPROTECTORS

The available information about the biological activity of chemicals which increase the life span of laboratory animals is summarised in Table 1. The specific manifestations of ageing are extremely varied, but they all reflect the disorganisation of the vital functions of the organs and tissues. The ageing of the organism is frequently regarded as a consequence of the accumulation of molecular injuries in cells and primarily in the genetic material[30]. The ideas concerning the harmful effects of free radicals are consistent with several at superficially incompatible hypotheses concerning the biological manifestation of ageing.

Table 1. Biological properties of geroprotectors.

2,6-Di-t-butyl-4-methylphenol (ionol)	food antioxidant[9], antiradiation agent[10], antileukaemic and anticarcinogenic agent[11–14], inductor of microsomal liver enzymes[14,15], substance reducing the frequency of chromosomal aberrations[16]
2-Mercaptoethylamine	antiradiation agent
Vitamin E	biogenic antioxidant, substance reducing the frequency of chromosomal aberrations[16]
6-Ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline	food antioxidant, inductor of microsomal liver enzymes[15], anticarcinogenic agent[13]
Nordihydroguaiaretic acid	antioxidant, inductor of microsomal liver enzymes[15]
3-Hydroxy-2-ethyl-6-methylpyridine.HCl	antiradiation agent[10], antioxidant[17]
2-(Dimethylamino)ethyl *p*-chlorophenoxyacetate (meclophenoxate)	substance preventing the accumulation of lipofuscin[18], stabiliser of biological membranes[19]
Dimethylaminoethanol	stabiliser of biological membranes[19]
Salicylates	stabilisers of biological membranes[19]
L-3,4-Dihydroxyphenylalanine	intermediate in the biosynthesis of adrenaline, used in the treatment of Parkinson's disease[20]
Sodium salt of ethylenediaminetetraacetic acid	prevents the formation of cross-links in macromolecules[21]
β-Aminopropionitrile	ditto (quoted after Comfort[2])
Corticosteroids	inductors of the biosynthesis of protein stabilisers of biological membranes[19], stimulators of the proliferation of cell cultures[22–24]
β-Diethylaminoethyl *p*-aminobenzoate (procaine)	active principle of the geriatric agent "Gerovital NZ", stimulator of the proliferation of cell cultures[27]
Ginseng and eleutherococcus extracts	substances influencing the secretory function of the adrenal cortex and the steroid hormone equilibrium[25], antioxidants, stimulators of cell division[26]
"Folcysteine U" complex	reactivates certain enzyme systems whose activity decreases wtih age, influences the SH/SS ratio[28]
"Decamevit", "Geroton", and "Amivit" polyvitamin complexes	used in geriatric practice, normalise metabolic processes, stimulate regeneration and haemopoiesis[29]

Free radicals play a significant role both in normal and in pathological vital processes. They have been detected in various tissues, subcellular structures, and in isolated

enzyme systems. It has been established that free radicals are active intermediate substrates in oxidation-reduction processes. It is suggested that about 60% of the overall concentration of free radicals in the cell, detected by ESR, is associated with electron transfer processes via the respiratory chain of mitochondria and with the formation of semiquinone radicals[31].

Free-radical states in other cell organelles have been inadequately investigated. About 20% of the overall concentration of free radicals is probably located in microsomes, where various extraneous substances are oxidised without phosphorylation and undergo detoxidation[32,33]. A correlation has been established between the amount of free radicals and the metabolic activity of the tissues[32,34]. Non-enzymatic oxidation processes involving organic molecules, mainly lipids, constitute another source of free radicals. Vitamin E, ascorbic acid, and other natural antioxidants regulate the normal level of these processes in the cell. Artificially created condition favouring non-enzymatic oxidation (irradiation, excess oxygenation) lead to pathological states[35]. Thus, following an increase in the amount and degree of unsaturation of fats in the diet, the life span of C3H mice decreased, and the incidence of mammary gland cancer rose, which may be due to the formation of toxic lipid peroxides. The introduction of α-tocopherol into the diet prevented these phenomena[36].

The possibility of intensifying free-radical reactions during ageing has been discussed in the literature, but systematic studies on these lines have not been undertaken. The concentration of free radicals in the organs of mice and rats of different ages has been investigated[37]; maximum concentrations have been recorded on the 12th and 43rd days of the animal's life, i.e. during the period of growth, after which there was a monotonic decrease. A comparative study of the organs of young (4 months old) and old (2 years old) rats of the "Vistar" strain revealed an increase with age in the concentration of free radicals in the liver and blood[38]. The free radical concentration in the brain tissue of 30 month old rats was higher than in 10 month old animals[39].

Numerous experimental data have shown that the physicochemical properties and functional characteristics of the molecules of information DNA and RNA change in the course of ageing[30,40-43]. Highly reactive free radicals of the type RO· and $RO_2^{\cdot}$ may play the role of agressive factors. The formation *in vivo* of lipid peroxides and unstable low-molecular-weight radical oxidation products, which may modify biological structures, causing, in particular, a decrease in the templet activity of DNA (quoted after Vilenchik[30]), has been demonstrated experimentally. Radical processes involving the oxidation of lipid components may be the cause of the breakdown of the integrity of membranes of subcellular particles. Lysosomes are present in the cytoplasm of almost all types of animal cells; they contain hydrolytic enzymes, which participate in the digestion of ballast substances, in the lysis of dead cells, etc. Damage to the lysosomal membrane *in vivo* can release the enzymes of the lysosomes into the cytoplasm and lead to the breakdown of its protein structures, damage to many important cell components, intensification of katabolic processes, and stimulation of the formation of connective tissue[19]. It is suggested that accumulation of the senile pigment lipofuscin is also associated with the degradation of lysosomes[44].

Inactive enzymes have been detected in the cells of old animals and in diploid cultures in the degradation phase[45-47], i.e. molecules retaining a specific structure which have lost their catalytic properties. The reason for the appearance of inactive enzymes may be structural defects in the templet, weakening of control by nuclear DNA over the synthesis of RNA[40], and postsynthetic modification of the proteins by the enzymes of lysosomes or free radicals.

Table 2. The life span of laboratory rodents.

Strain of animals	Sex. no. of animals	Median life span, weeks	Life span, weeks: average ± s.d.*	Life span, weeks: maximum	Refs.
LP	males, 77	107	103±2.6	142	63
	females, 51	102	99±2.7	127	
129	males, 54	126	117±4.2	154	63
	females, 95	111	104±3.1	148	
DBA/2	males, 67	86	82±3.7	125	63
	females, 51	85	81±3.2	118	
CBA	males, 17	111	107±3.9	125	63
	females, 33	94	91±2.9	116	
C57BL/10	males, 39	124	118±4.1	165	63
	females, 35	104	99±4.4	141	
C3H	males, 29,	112	113±5.3	157	63
C3H·K	males, 25	115	104±5.0	131	
(LP × 129) F_1	males, 54	120	122±3.1	169	63
	females, 77	118	118±2.5	158	
(LP×DBA/2)F_1	males, 42	123	121±4.4	163	63
	females, 43	95	93±3.7	152	
(129×DBA)F_1	males, 47	139	135±4.0	186	63
	females, 58	119	119±3.2	169	
(CBA×C57BL/10)F_1	males, 40	126	142±0.7	143	63
	females, 29	104	141±0.9	142	
(LP×C57BL/10)F_1	males, 42,	130	125±3.9	185	63
	females, 48	120	123±3.4	176	
(A×C57BL/10)F_1	males, 42	116	117±3.3	152	63
	females, 72	127	125±2.7	186	
(CBA×C3H·K)F_1	males, 21	111	109±3.7	133	63
(C3H×C3H·K)F_1	males, 36	122	120±2.7	147	63
CBA/J	males 73	—	75.0±2.5	—	64
	females, 75	—	75.0±2.0	—	
DBA/2	males, 75	—	101±3.2	—	64
	females, 80	—	102±3.0	—	
129/J	males, 79	—	97±2.9	—	64
	females, 78	—	92±3.2	—	
C57BL/6J	males, 74		96.5±2.9	—	64
	females, 75		99±2.9	—	
AKR/J	males, 39	—	46.5±2.0	—	64
	females, 72	—	39.4±1.2	—	
C3H	males, 40	—	78.7±3.4	101.5	65
	females, 40	—	77.3±4.7	103.0	
CD—1 **	males***, 86	74.3	74.5	—	66
	females, 86	99.5	92.8	—	
Sprague-Dowley rats	males	—	108	172	quoted after (Ref.61)
		101	—	167	
Ditto	?	—	99±31	—	61

*s.d. = standard deviation.
**non-inbred strain.
***germ-free conditions.

The influence of antiradical preparations on the level of oxidation-reduction reactions in the tissues of the organism can be inferred from the change in the antioxidant activity (AOA) of lipids, which characterises the ability of lipid extract to counteract oxidation and is caused by the presence of natural antioxidants. Measurements of AOA of mouse liver lipids during ageing showed that it steadily decreases with age and that the rate of its variation is not the same for different strains of animals[48]. In radiation sickness, stress states (starvation, supercooling), and poisoning a decrease of AOA is observed, as in ageing. The development of these processes may be retarded and even prevented by the introduction of substances which increase the level of anti-oxidant activity. Natural and

synthetic antioxidants (tocopherol, ionol, 2-ethyl-3-hydroxy-6-methylpyridine), certain hormones (hydrocortisone, adrenaline), and preparations belonging to the class of non-specific adaptogens (eleutherococcus) are able to alter the level of AOA of tissue lipids, i.e. they can influence directly or indirectly the intensity of radical oxidation processes in the organism [49-53].

The possibility of preventing or effectively retarding a wide variety of undesirable deviations, which inevitably occur in the living organism, and also the prophylaxis and liquidation of pathological states have a bearing on the problem of the prolongation of the life span. The increase of the incidence of illness in middle age, which may be associated with the activation of latent viruses, is considered as one of the manifestations of ageing [54]. Effective geroprotectors (antioxidants—ionol and ethoxyquin) have a set of favourable properties: anticarcinogenic activity [12-14], the ability to prevent the accumulation of chromosomal aberrations [16], and antileukaemic activity [11]. Ionol is used in the treatment of bladder tumours and radiation-induced and trophic lesions of the skin [56,57].

It is well known that the toxic effect of chemical agents and medicinal preparations increases with the recipient's age. The effects of ionol, nordihydroguaiaretic acid, propyl gallate, and ethoxyquin on the activity of oxidative enzyme systems of liver microsomes, which metabolise extraneous chemical compounds, medicinal preparations, poisons, etc., have been studied [15]. The introduction of ethoxyquin into the diet of rats aged 81–440 days increased by a factor of two the enzymatic activity of the microsomal fraction; ionol and nordihydroguaiaretic acid exhibited a somewhat lower inducing capacity; propyl gallate did not exhibit the properties of an inductor and did not increase the life span of rats. Preliminary administration of ethoxyquin to rats decreases the toxic effect of carbon tetrachloride, increasing the rate of its conversion into CO_2. [58] Possibly the induction of the detoxicating enzyme system in microsomes constitutes the molecular mechanism of the mobilisation of the vital forces of the organism against the harmful effect of the chemical components in the environment.

The set of favourable properties of antiradical preparations may serve as a basis for the future development of medicinal compositions designed to reduce the rate of ageing in man.

III. COMPARATIVE ASSESSMENT OF THE EFFECTIVENESS OF GEROPROTECTORS

The wide-scale employment of laboratory rodents in the study of ageing implies the assumption of a definite similarity between the ageing processes in these species and in man. To estimate the rate of the ageing process and the effectiveness of geroprotectors, mortality indices for the population are used. The following characteristics are usually analysed: the average and maximum life span; the "median" life span, i.e. the age corresponding to 50% mortality; the law of the frequency distribution of deaths; the relative death rate linked to age by a logarithmic relation (the Gompertz index); the "expected life span". [59]

A correct study of the percentage survival of laboratory rodents is possible when not less than 800–1000 animals are used. About 3000 mice of the SAS/4 strain of both sexes have been observed from birth to death [60]. The average life spans of the males and females did not differ, amounting to 103.8 weeks. The Gompertz relation held over the range 50–100 weeks, while at more advanced ages the mortality index increased more slowly. A logistic function of the type

$$\mu = 122 \cdot 10^{-5} + \frac{3.3 \cdot 10^{-5} e^{0.0632t}}{1 + 23 \cdot 10^{-5} e^{0.0632t}},$$

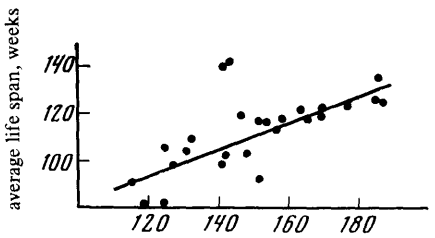
where $\mu = -(1/n)(dn/dt)$ is the relative death rate and n the number of living individuals whose age is t, is suitable for a complete description of the percentage survival curve. The distribution of life spans proved to be asymmetric.

The study of the percentage survival of laboratory Sprague-Dowley rats was continued for five years [61]; 747 animals were used in 18 experiments, 7 of which were performed in a germ-free medium and the remainder in the usual vivarium with careful maintenance of cleanliness and constant living conditions. The average life spans were virtually the same in all the experiments, the mean amounting to 692 ± 22 days. Analysis of the frequency distribution of deaths showed that, compared with the normal distribution, there is an excess of short-lived individuals. For old rats aged 800–950 days, the expected life span remains constant and the relative death rate decreases. The decrease of the Gompertz index by a factor of two at an age of 1060 days compared with an age of 450 days was observed also for CAF_1 hybrid mice [62].

In the majority of experimental studies groups of 100 and fewer animals are usually employed, which leads to appreciable differences between the percentage survival indices for animals of the same strains investigated in different laboratories and even in the same laboratory but at different times. Table 2 presents data for the life spans of mice belonging to 8 inbred strains and 8 first generation hybrid groups, one non-inbred strain of mice (CD-1), and Sprague-Dowley rats. Comparative analysis of the data in Table 2 permits the following conclusions: (1) the life span of male mice is greater by 10–12% than that of female mice, although there are exceptions [67,68]; (2) the life span of first generation hybrids is longer than for mice of the parent strains; (3) the average life span is close to the median value, i.e. the two parameters can be used to an equal extent; (4) the greatest differences between the life span are observed for the inbred strains 129 and AKR (by a factor of 2.7); (5) the average life spans obtained in different laboratories differ for strains 129, DBA/2, and the genetically similar strains C57BL/6, and C57BL/10 approximately by a factor of 20% and for strains CBA and CXH by 40%. A study of the life spans of C57BL male mice in four independent experiments in the same laboratory showed that the median and maximum life spans differ by 34 and 17%, and the source from which the animals had been obtained is significant [69].

In selecting the animals to be subjected to protracted survival tests, preference should be given to the following inbred strains with a stable genotype: 129, CBA, C57BL, C3H, C3HA, LP, BALB/c, and SWR; it has been shown that the incidence of malignant tumours in these strains or first generation hybrids is low [61,63,68,70]. The advantages of gnotobiology are not evident: a decrease of the life span of the animals under germ-free conditions is sometimes observed [66,71-73]. Since the average life span depends significantly on environmental and dietary factors, we must assume that the chemicals employed as geroprotectors really retard the ageing process only when an increase in the maximum life span is observed compared with the control group of animals of the same breed. The treatment of quantitative data for the percentage survival of mice of different inbred strains and first generation hybrid groups [63] showed that there is a linear relation

between the average and maximum life spans under optimal living conditions (see Figure). The regression equation is $y = 24.6 \pm 0.57x$, with a correlation coefficient $r = 0.85 \pm 0.055$. This relation implies that, when ageing is retarded, a decrease of mortality is to be expected for the entire population, which leads to a rightward shift of the percentage survival curve.



Regression line for the average and maximum life spans of mice according to Smith et al.[63]

The possibility, in principle, of increasing the life span of laboratory animals by means of certain chemicals as dietary additives in small amounts was demonstrated for the first time in a number of studies[5,6,8]. When inhibitors of radical reactions with the properties of antiradiation agents and antioxidants (2,6-di-t-butyl-4-methylphenol, ammonium diethyldithiocarbamate, 6-ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline, and α-tocopherol) were added to the diet in amounts of 0.25–1 wt.%, the percentage survival in the test groups after 20 months amounted to 61.66, 74, and 13% compared with 9% in the control[74].

The results of subsequent investigations are combined in Table 3. The increase of the average and maximum life spans varies in the range 13–50% and 11–58%. The influence of the most effective chemicals is compared with the results obtained in studies by McCay[4], who used prolonged partial starvation of young rats as a factor retarding their growth and development and leading to an increase of their life span. In experiments carried out in 1934 the life span of test individuals exceeded by 78% the maximum life span of the control. In repeated experiments the increase of the life span varied from 22 to 32%. Nikitin and coworkers[82], who reproduced McCay's experiments, found that the average life span of test animals increased by 39% and the maximum life span by 47%.

Despite the fact that the search for chemicals retarding the ageing process has continued for about 20 years as a scientific discipline, the list of active compounds includes no more than 20 items. The principal cause of the slow development of this field is lack of knowledge of the primary causes and mechanisms of ageing. In selecting geroprotectors, the investigators were forced in most cases to employ more or less plausible hypotheses as a basis. The preferential use of laboratory rodents makes the experiments long, expensive, and laborious, and their results cannot be predicted as long as data for the mortality of a control group of animals have not been secured.

Attempts were made in a number of investigations to develop biological methods making it possible to follow the rate of ageing by procedures which are not based on mortality indices alone. Several tests have been proposed to characterise the biological age of rats. When the rate of ageing is accelerated by fractional irradiation with X-rays, comparison of the calendar and biological ages using the method proposed by the authors showed that the test group was "older" than the corresponding control group. The opposite findings were obtained when ageing was retarded by periodic feeding of Na_2-EDTA.[76,83,84] The fundamental studies[85,86] in which changes in enzyme induction associated with ageing are investigated as a biochemical expression of ageing are interesting and promising.

Table 3. Influence of chemical geroprotectors on the life span of laboratory rodents.

Compound	Dose	Strain of animals, sex, age at beginning of experiment	Difference relative to control, %		Refs.
			avergae life span	maximum life span	
2-Mercaptoethylamine.HCl	0.5 wt.%	LAF_1 male mice	12.8	–	75
"	1.0 wt.%	ditto	29.0	–	
2,6-Di-t-butyl-4-methylphenol (ionol)	0.25 wt.%	"	17.6	–	75
Ditto	0.5 wt.%	"	44.6	–	
6-Ethoxy-2,2,4-trimethyl--1,2-di-hydroquinoline (ethoxyquin)	0.5 wt.%	C3H male mice, 3 months	18.0	25.0	3,65
Ditto	"	C3H female mice, 3 months	20.0	26.0	
Na_2 salt of EDTA	50 mg day^{-1}	female rats, 320 ± 10 days	18.7	–	76
2-(Dimethylaminoethyl) *p*-chlorophenoxyacetate (meclophenoxate)	60 mg kg^{-1}	Swiss male mice, 8.6 months	27.3	26.3	77
Dimethylaminoethanol	7 mg kg^{-1}	A/J male mice, 604–664 days	49.5	10.9	78
L-3,4-dihydroxyphenylalanine	40 mg/g of diet	Swiss male mice, 4–5 weeks	34.0*	–	79
3-Hydroxy-2-ethyl-6-methyl pyridine-HCl	1.5 mg day^{-1}	SHK female mice, 2 months	34.0	12.5	80
Ditto	3 and 6 mg day^{-1}	SHK female mice, 8–8.5 months	23.2	58.0	80
Ginseng and eleuterococcus extracts	–	white rats	21 and 16	–	26
Polyvitamin complexes: "Decamevit"	–	rats	3.3	–	81
"Geroton" and "Vitavit"	–	"	13.3	–	81
Complex of polymicroelements	–	"	23.3	–	81

*At 18 months of age.

Apart from laboratory rodents, populations of the fruit fly *Drosophila melanogaster* are frequently used to investigate the ageing process and to select geroprotectors. Its use has advantages in the sense that in the tissues of the adult insect there are no dividing cells, i.e. the death of the organism coincides with the death of its cells. The life span of the adult insect depends on the conditions in the medium, the population density, and the rate of preimago development[44,87,88]. The average life spans of various strains differ significantly: it is 40 days for the short-lived mutant strains Hk^1P and Sh^5,[89] while for wild species it is almost twice as long[19]. The older the

parents the shorter the average and maximum life spans of the offspring. The life span of the second generation hybrids is somewhat shorter than that of F_1 hybrids[90]. It is possible to use F_2 hybrids in those cases where a large initial population of individuals with the same life spans is required for the experiments.

As for laboratory rodents, the retardation of ageing should lead to a decrease of the mortality of the entire population, to an increase of the maximum life span, and to a rightward shift of the entire mortality curve. Among the 38 compounds of different classes which were added to the diet in different concentrations, positive effects were found for only a few (Table 4). The majority of the compounds tested were selected on the basis of their known or postulated ability to stabilise cell or lysosome membranes towards decomposition *in vivo* and *in vitro*[91]. A reliable increase of the average life span of males was achieved under the influence of corticosteroids, salicylic acid derivatives, and meclophenoxate. The greatest increase in the maximum life span (by 42%) was attained when a mixture of salicylsalicylic acid and aspirin was used.

Table 4. The influence of chemical geroprotectors on the life span of *Drosophila melanogaster*[19,92].

Compound	Dose, mg/100 ml of medium	Strain of insect, sex	Difference relative to control, %	
			average life span	maximum life span
Hydrocortisone acetate	10	(*Canton S* × *Oregon 2S*)F_1 males	38	16
		females	21	18
Cortisone acetate	18.8	(*Canton S*) males	43	31
Deoxycorticosterone acetate	0.5	females	18	13
		males	21	21
Triamcinolone(9α-fluoro--16α-methylhydrocortisone)	4	males	18	5
		females	19	16
Aspirin	250	(*Canton S* × *Oregon RS*)F_1 males	22	27
		females	13	16
3:1 salicylsalicylic acid–aspirin mixture	490	males	24	18
Ditto	162	females	38	42
Salicylamide	650	males	17	22
		females	12	27
Meclophenoxate	120	males	7	15
		females	39	23
Ionol	0.001%	males	30	–
		females	16	–
Butylhydroxyanisole (BHA)	0.01%	males	12	–
		females	5	–

The procedure whereby biologically active substances retarding ageing are selected can be greatly shortened by employing populations of microscopic polycellular nematodes (*Caenorhabditis origgsae*) and rotifers (*Bdelloid rotifer*)[93–98], whose life span is close to 1 month and which can be grown simply and in large amounts without much expense. The presence of α-tocopherylquinone in the culture medium retarded the ageing process of nematodes whose age at the beginning of the experiment was one day, and increased by 30% the average life span. A positive effect was not observed if the age of the animals was 20 days, since irreversible changes associated with ageing had occurred[99]. The influence of inhibitors of the biosynthesis of proteins, antimetabolites, and cytostatic agents on the life span of rotifers has been studied[100]. The following inhibitors of biosynthesis were found to retard ageing: actinomycin D, streptomycin, Acridine Orange, tetracycline, and chromomycin A_3.

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Progress in this field of experimental gerontology depends on scientific advances in the understanding of the principal mechanisms of ageing. The next urgent task is to combine the search for substances "capable of protecting the cells from senile changes in a manner similar to that occurring on restricting the diet"[87] with improved methods for recording the rate of ageing.

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The Solvated Electron in Polar Organic Liquids

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The spectroscopic characteristics and the mechanism of the motion of solvated electrons in polar organic liquids are examined. It is shown that the part of the spectrum where solvated electrons absorb is determined by the polarity of microregions in the liquid. The intensity and half-width of the absorption band depend on the region of the spectrum in which absorption occurs. The theoretical concepts concerning the nature of the solvated electron and the mechanism of its motion are considered. The bibliography includes 65 references.

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I. INTRODUCTION

The study of excess electrons in liquids (solvated electrons) is of particular interest for the understanding of their behaviour as chemically reactive species giving rise to a wide variety of reactions and determining the fundamental step in electrochemical, radiation-chemical, and other processes. These processes are determined by the nature of the localised state and the diffusion characteristics of the electrons. The possibility of the dissolution of alkali metals in ammonia was first discovered by Weyl[1]. Kraus[2] suggested that the colour of the resulting solution is associated with the solvated electron formed on association of the metal atom to the cation and an electron. A brief unstable colour was also observed on dissolution of alkali metals in polar solvents, for example alcohols, at a low temperature[3]. By analogy with ammonia, it was attributed to solvated electrons. A new stage in the study of solvated electrons began after the detection of hydrated electrons by pulse radiolysis[4]. The subsequent employment of this method made it possible to obtain quantitative characteristics of solvated electrons (e_s) in various liquids where their lifetime amounts to a fraction of a second. The study of such electrons in a wide variety of organic liquids led to fundamentally new results, which are important for the understanding of the nature of the solvated state of the electron.

The principal method for detecting solvated electrons involves the measurement of absorption spectra, which characterise mainly the localised state of e_s. There have been only a limited number of investigations of the relaxation currents associated with the motion of solvated electrons. For this reason, the mechanism of their transport in polar liquids has been least thoroughly studied compared with their other characteristics. The spectroscopic characteristics of solvated electrons have now been measured in a large number of pure organic liquids, both polar and non-polar, and in mixtures of organic liquids with different proportions of the components; the experimental wavelength range in which solvated electrons absorb extends from 250 to 3000 nm. The temperature range of the measurements of the e_s spectra extends from the temperature of liquid helium[5] to temperatures in excess of critical values (in the case of water)[6]. The influence of pressure up to several kilobars on the absorption spectra of solvated electrons has been studied. The time interval corresponding to the investigation of the formation of and changes in the absorption spectra of solvated electrons is between 10^{-11} and 10^{-3} s. In some cases stable spectra of solvated electrons were recorded. Much attention has been devoted to the investigation of a large number of reactions of solvated electrons with various additives and also to the investigation of the influence of certain compounds which do not interact chemically with e_s, on the ways in which the latter are stabilised, which is reflected by a change in the characteristics of the absorption spectra. Systematic accounts of the results have been given in reviews and monographs[7-12] and reference data have been published[13,14].

II. CERTAIN THEORETICAL MODELS OF THE SOLVATED ELECTRON

Despite the abundance of experimental data, there is at present no generally accepted theoretical model which would explain all the experimental results for solvated electrons. The current aim of the main fundamental approaches to the understanding of their nature is to explain the principal parameters of the optical absorption spectra of solvated electrons, namely the half-width of the absorption band, its asymmetry, intensity, the coefficient of the temperature shift of the wavelength of the absorption maximum (λ_{max}), and the dependence of the position of λ_{max} on the macroscopic and microscopic characteristics of the medium.

The theoretical models discussed in various studies can be conventionally divided into two groups. In those of the first group an attempt is made to calculate, by considering real characteristics of the liquid, the parameters of the potential well in which the electron is localised, the distribution of the discrete energy levels in it, and the limit of the continuous spectrum of levels. In models of this group account can be taken of various types of interactions between the electron and the condensed medium. The simple polaron model considers the medium as a macroscopically continuous dielectric[15-18]. In semicontinuous or molecular-cavity models account is taken of

the molecular structure of the solvent, in contrast to the polaron model[19,20]. Consideration of the excess electron in a polar medium within the framework of the adiabatic approximation with simultaneous examination of the electronic energy and the energy of solvent rearrangement has proved to be the most successful approach[19]. In structural models it is assumed that the electron is bound to the nearest solvent molecules sufficiently strongly to neglect long-range interactions and the localisation of the electrons at several molecules[21], dimers, trimers[22], clusters[23], and structural defects[24] is considered. The principal achievement of this group of studies is agreement between the theoretically calculated and experimental λ_{max} for solvated electrons in water and ammonia. On passing to more complex organic molecules, such agreement cannot be attained. In these investigations the spectra are interpreted almost exclusively as due to a transition between two discrete levels, usually the $1s \rightarrow 2p$ transition (i.e. the electron remains bound in the excited state).

The other approach involves the selection of a form of potential whereby an agreement between the theoretically calculated absorption band of solvated electrons and the experimental band can be achieved by a suitable choice of a definite number of parameters. Thus, when the hydrogen-like potential is used and two parameters are adjusted, it is possible to reach[25] complete agreement between the calculated and experimental absorption curves for solvated electrons in various liquids over a wide range of pressures and temperatures. However, the parameters obtained in the mutual adjustment of these spectra can be in no way related to the real characteristics of the liquid and therefore the predictive value of this approach is slight. The experimental data obtained in recent years leads to the conclusion[26,27] that optical absorption is determined mainly by the transition to a continuous spectrum. On the basis of this assumption, it can be shown[28] that, by specifying the simplest form of the potential curve, namely a rectangular well, it is possible to achieve a satisfactory agreement between the theoretical and experimental absorption curves when certain parameters are chosen. Certain important characteristics of solvated electrons have been calculated[29] from the shape of their absorption line using threshold formulae and it was concluded that the lower energy side of the absorption band corresponds to photoionisation, the effective interaction in the final state being short-lived.

Evidently the development of theoretical concepts concerning the nature of the solvated electron is determined in both approaches by the possibility of a more specific allowance for the fundamental forms of interaction between the electron and the liquid medium. In its turn this entails a systematic treatment of the available experimental data and the determination of the general characteristics of the behaviour of these electrons in various liquids.

III. SPECTROSCOPIC CHARACTERISTICS IN POLAR LIQUIDS

In a number of studies, attempts were made to relate the spectroscopic characteristics of the solvated electron to the properties of the liquid in which it is solvated. A correlation has been observed[30] between the static dielectric constant (D_{st}) and λ_{max} in methanol, ethanol, propanol, and ethylene glycol. However, measurements of the absorption spectra of solvated electrons in twenty straight-chain and branched-chain alcohols[31,32] showed unambiguously that no such correlation exists. These investigations showed, for alcohols, that there is also no correlation between λ_{max} and the fundamental parameter of the polaron theory $\beta = 1/D_{opt} - 1/D_{st}$. Analysis of the absorption spectra of solvated electrons in a large number of organic liquids of different structures leads to the conclusion[31,33] that the localised state of the electron in a polar liquid is probably determined by the interaction with the polar groups of a small number of molecules of the liquid.

It is noteworthy that the question of whether or not λ_{max} is determined by the interaction of the electron with a large number of molecules of the liquid (i.e. by the dielectric characteristics of the medium) or with the first solvation layer (i.e. by short-range forces) cannot be answered by studying two-component systems[34,35], since a gradual substitution of one mixture component by another also produces a smooth change in the dielectric constant. For this reason, the spectra of solvated electrons were studied by pulsed radiolysis in monoethanolamine (MEA), a bifunctional compound, and in an equimolar ethanolamine mixture[36]. MEA and the mixture have similar chemical compositions but differ appreciably in their dielectric constants: $D_{st} = 57.7$ for MEA and $D_{st} = 10.5$ for the mixture at 20°C. The wavelength corresponding to the optical absorption maximum of solvated electrons in MEA is 910 nm [36]; it occupies an intermediate position between λ_{max} for ethanol (700 nm [30]) and ethylamine (1300 nm [37]) and is close to λ_{max} for the mixture (880 nm), although the dielectric constants of MEA and the mixture differ by a factor greater than 5. Thus the position of the absorption maximum of solvated electrons for liquids having similar chemical compositions is determined by the presence of functional groups, in the present case OH and NH_2, and is independent of the macroscopic characteristics of the liquid.

For liquids with appreciably different molecular structures, it is also impossible to observe a correlation between λ_{max} and D_{st}. The same applies to the parameter $D_{st}\rho$ (where ρ is the density), which is correlated with the changes in λ_{max} or E_{max} (the energy corresponding to λ_{max}) as a function of pressure and temperature in alcohols but not in other liquids[38]. An attempt to take into account in a more complex manner the influence of the structure of the liquid on the position of E_{max} has been made[39]. Assuming that the structure of the liquid plays a major role in determining E_{max}, the author calculated the values of the correlation parameter g_c in the Kirkwood equation for various liquids:

$$[(D_{st.} - 1)(2D_{st.} + 1)/9D_{st.}](M/\rho) = (4\pi N/3)[\alpha + (g_c\mu^2/3kT)], \quad (1)$$

where M is the molecular weight, α the molecular polarisability, and μ the dipole moment. Values of g_c greater than unity indicate a greater local polarity in microscopic regions within the liquids than might have been expected from the molecular dipole moment.

A satisfactory correlation has been observed between E_{max} and the parameter $D_{st}\rho g_c^3\alpha_p$ (α_p is the polarisability of the polar group in the molecule) for a number of amines, ethers, alcohols, water, and ammonia[39]. However, subsequent measurements of the spectra of solvated electrons in amides[40] failed to confirm the general applicability of the observed relation. For example, E_{max} for *NN*-dimethylacetamide is smaller by a factor of three than might have been expected from the relation. This is because the parameter $D_{st}\rho g_c^3\alpha_p$ is largely determined by the macroscopic characteristic D_{st}; since amides are characterised by relatively high values of D_{st} (30–40), there is a sharp

inconsistency between the similar values of E_{max} observed for amides and for example weakly polar amines, on the one hand, and the widely different values of $D_{st}\rho g_c^3 \alpha_p$ for the same liquids, on the other.

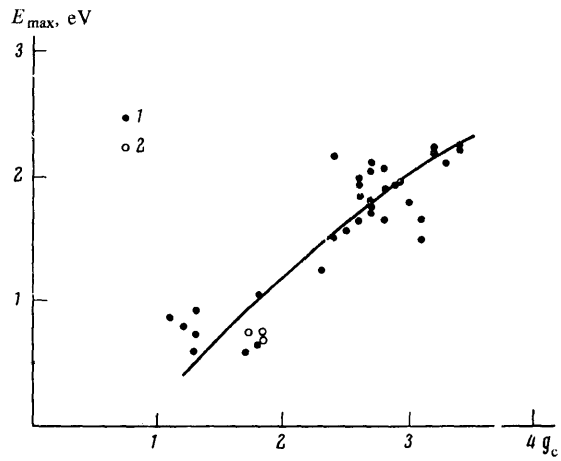

Figure 1. Variation of E_{max} (e_S) with the correlation parameter g_C of polar liquids: 1) liquids considered by Freeman[39]; 2) liquids investigated by Galvas et al.[40].

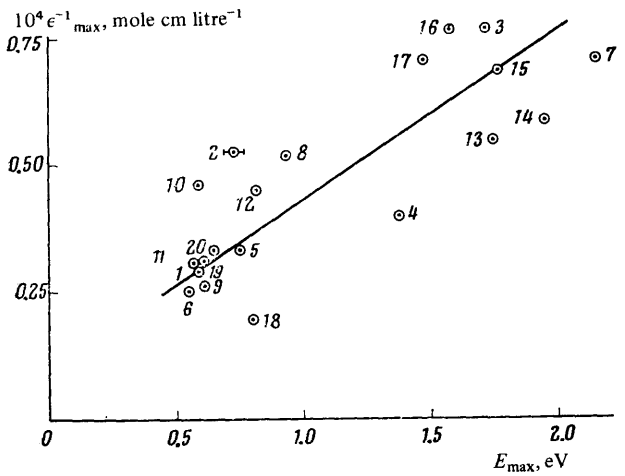

Figure 2. Variation of ϵ_{max} for the solvated electron with E_{max} in different liquids: 1) hexamethylphosphoramide[41]; 2) dimethyl sulphoxide (the upper limit of ϵ_{max} calculated from the data of Cooper et al.[63] is quoted); 3) 2-methoxyethanol[40]; 4) ethyl methyl ketone[46]; 5) squalane[64]; the remaining points were calculated from data quoted by Dorfman and Jou[42]; 6) ethyl ether; 7) ethylene glycol; 8) ethylenediamine; 9) tetrahydrofuran; 10) methyltetrahydrofuran; 11) diethylamine; 12) 1,3-propylenediamine; 13) water; 14) methanol; 15) ethanol; 16) 1-propanol; 17) isopropyl alcohol; 18) ammonia; 19) dimethoxyethane; 20) diglyme.

It was shown above that macroscopic characteristics have only a weak influence on the mechanism of the formation of the solvated electron and E_{max}. If the interaction of the electron with the nearest polar groups is regarded as the main one, a correlation may be expected between E_{max} and g_C. Indeed, Fig. 1 shows that, for all the liquids considered[39,40], including amides (open circles), the same functional relation holds between E_{max} and g_C.

There are few experimental data for the variation of the shape of the e_S absorption band on passing from one liquid to another. For ammonia[35], hexamethylphosphoramide[41], and 2-methoxyethyl ether[42], the absorption band is satisfactorily represented by a combined Lorentzian–Gaussian profile; the long-wavelength component of the absorption band is then described by the Gaussian function and the descent from the maximum in the direction of short-wavelengths obeys the Lorentzian function. In other liquids such analysis is difficult, particularly because of the inadequate accuracy of the recording of the e_S spectrum. However, it is possible to find a relation between simpler parameters characterising the spectrum and the position of the spectrum on the wavelength scale. Fig. 2 presents the variation of the reciprocal of the extinction coefficient at the maximum (ϵ_{max}) with E_{max}. Evidently, the extinction coefficient increases for all liquids with decrease of E_{max}. If one remembers that the oscillator strength of the e_S absorption band changes little (in the range 0.5–0.9), then the above finding reflects the fact that the e_S infrared absorption bands are narrower and more intense than the bands at short wavelengths.

IV. INTERACTION WITH POLAR LIQUIDS

Thus the region of the spectrum in which the solvated electron should absorb and the spectral characteristics can be predicted beforehand, albeit very approximately, for any organic liquid, subject to the condition that the electron is solvated in this liquid, i.e. does not react with the molecules of the liquid before solvation. The lifetime of the solvated electron in a particular organic liquid is usually inferred from the rate constant for the reaction of the hydrated electron with the molecules of the liquid. However, it is clear from the foregoing that in each liquid the solvated electron exhibits specific properties which do not allow the simple assumption that the properties are the same as those of the hydrated electron.

The factors governing the stabilisation of electrons in various organic liquids can be found by considering the results of a study of the interaction of low-energy (~1 eV) electrons with organic molecules in the gas phase[43,44]. This shows[46] that solvated electrons are formed in liquids whose molecules interact with electrons in the gas phase to form extremely short-lived negative ions ($10^{-15} \leq \tau \leq 10^{-12}$ s) and are characterised by a negative electron affinity. The rate constants for the e_S annihilation reactions in these liquids are $\leqslant 10^7$ litre mole^{-1} s^{-1}.

The results of the gas-phase measurements have been compared[44] with the rate constants for the interaction of hydrated electrons with the molecules of the above organic compounds in aqueous solutions. This leads to conclusions which are difficult to account for, for example when ketones are considered. Forming only extremely short-lived ions in the gas phase, they nevertheless react with hydrated electrons and the reaction is characterised by a high rate constant ($k = 6 \times 10^9$ litre mole^{-1} s^{-1}). Without considering in detail the mechanism of this reaction, the above considerations might have suggested that solvated electrons can be detected in pure liquid ketones, in view of the results of the gas-phase measurements. Indeed, a species has been detected in ethyl methyl ketone, whose

properties, such as the position of the absorption band (λ_{max} = 900 nm), its shape, its extinction coefficient ($\epsilon_{max} = 2.5 \times 10^4$ litre mole^{-1} cm^{-1}), and its half-width (0.5 eV) are quite similar to the spectroscopic characteristics of solvated electrons in other organic liquids [33,45]. Here we may note that the mobility of solvated electrons in ethyl methyl ketone (EMK) greatly exceeds the mobility of molecular ions in the same liquid [46]. Similar results were obtained in other investigations [40]. The rate constant for the reaction of electrons solvated in ethanol with dimethylformamide ($k = 1.1 \times 10^9$ litre mole^{-1} s^{-1}) suggests that in pure dimethylformamide (DMF) solvated electrons are not formed (the lifetime $\tau < 5 \times 10^{-11}$ s). In practice it was found that solvated electrons with an infrared spectrum having a lifetime of about 1 μs are formed in pure DMF. Naturally the specific features of the condensed state, particularly the association of molecules in the liquid, have an appreciable influence on the mechanism of the reaction of solvated electrons with the organic liquid molecules, as will be shown below.

Depending on the method of generation, solvated electrons can be obtained both in equilibrium with the surrounding medium (electrochemical generation, dissolution of metals) and in a non-equilibrium state (radiation-induced generation and photoionisation). In the latter case the lifetime of the solvated electron can be determined by its recombination with an ionised parent molecule or with radiolysis (photolysis) side products. However, for any method of generation, the maximum possible lifetime of the solvated electron is determined by the rate of its reaction with the molecules of the organic liquid in which it was solvated.

Despite the extensive experimental data obtained in studies of the kinetic characteristics of solvated electrons in various organic media, a comparative study of the influence of the molecular structure of liquids on the reaction of the electron with the medium has not been made. Nevertheless, the latter is one of the most important reactions [8,9]. The influence of the structure of the matrix on this reaction was studied for aliphatic monohydric alcohols with different hydrocarbon chain lengths and also for glycols and glycerols [46,47]. Using the method of pulse radiolysis, measurements were made of the rate constants for the reaction

$$ROH + e_s \xrightarrow{k} RO^- + H. \qquad (2)$$

Fig. 3 presents the values of k as a function of the number of carbon atoms n in the hydrocarbon chain in alcohols, iso-alcohols, and glycols at room temperature. The values of k for methanol and ethanol were taken from Rzad and Fendler [48] and a second, lower value for methanol from Iha and Freeman [49]. The Figure shows that k increases monotonically with increase of the hydrocarbon chain length and the constant is higher for alcohols with the iso-structure and glycols than for straight-chain alcohols. In conformity with this relation, $k = 2.4 \times 10^5$ litre mole^{-1} s^{-1} was obtained in glycerol, which agrees with the value quoted by Kajiwara and Thomas [50], but greatly exceeds the k values for propanol and propylene glycol.

Examination of the possible reaction mechanisms leads to the conclusion that the electron most probably reacts with monomeric matrix molecules which are not associated by hydrogen bonds [46]. In this case the activation energy for the reaction is related to the dipole relaxation of the liquid molecules, leading to the dissociation of the hydrogen bond, and amounts to several kcal mole^{-1}. The dependence of the rate constant on the hydrocarbon chain length of the alcohol molecules can be naturally explained, since it is known [51] that in the lower alcohols–higher alcohols series the degree of association diminishes. This also happens on passing from straight-chain to branched-chain alcohols, in agreement with the experimental results.

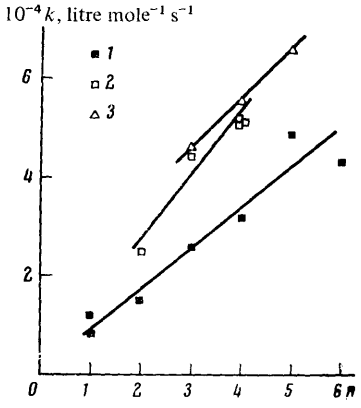

Figure 3. Variation of k with the number of carbon atoms n in the hydrocarbon chain: 1) straight-chain alcohols; 2) glycols (ethylene glycol, 1,2-propylene glycol, and 1,3-, 1,4-, and 2,3-butylene glycols); 3) iso-alcohols (isopropyl, isobutyl, and isopentyl alcohols).

The change in the rate constant on increasing the number of hydroxy-groups per molecule in the series 1-propanol, 1,2-propylene glycol, and glycerol is of interest, these being 2.6×10^4, 4.5×10^4, and 2.4×10^5 litre mole^{-1} s^{-1} respectively. When the rate constant is recalculated relative to the concentration of OH groups, it is found to increase only for glycerol: 2.6×10^4; 2.3×10^4; 8×10^4. This implies that the concentration of unassociated hydroxy-groups does not change on passing from the alcohol to the glycol and increases for glycerol, but the degree of association increases in this sequence with the corresponding variation of viscosity (2.2, 45.6, and 960 cP). Experimental confirmation of this would constitute valuable support for the hypothesis that the solvated electron reacts with the medium.

However, one cannot assume that the reaction of solvated electrons with monomeric molecules is diffusion-controlled, since, when the rate constant is calculated in terms of the concentration of monomeric molecules, which constitute only a few per cent of the total number of molecules, it is nevertheless still several orders of magnitude lower than the diffusion limit.

V. THE CHARACTERISTICS OF TRANSPORT IN POLAR LIQUIDS

Despite their importance, the reactions of solvated electrons with the molecules of liquids by which they are solvated have been studied much less than those of solvated electrons with the acceptors introduced into the liquids. Being one of the most chemically reactive species, the solvated electron reacts in many instances with organic molecules at rates controlled by the diffusion

limit. The rate constants for these reactions are determined by the mobility of the solvated electron and can be calculated using the latter. The study of solvated electron transport phenomena is important for the elucidation of the mechanism of the motion of electrons in non-ordered liquid media, for the determination of the nature of the interaction of solvated electrons with acceptors, and for the elucidation of the mechanism of oxidation-reduction reactions.

The mobilities of solvated electrons were previously measured reliably only in water[52,53] and in ammonia[54]. In water the mobility $\mu(e_S)$ of the solvated electrons generated by the ionising radiation pulse was obtained from electrical measurements, since the mechanism of the ionic process initiated by ionising radiation in water is known in detail. From this standpoint, organic liquids have been much less thoroughly investigated. Furthermore, in polar organic liquids the lifetime of the solvated electron is as a rule 10^{-4}–10^{-8} s owing to its interaction with the molecules of the liquid or the acceptor, and it is impossible to use standard methods for the determination of mobilities by measuring the time of flight of the electron between the electrodes. For this reason, a method has been developed for the measurement of the mobility of solvated electrons in which pulse measurements of their optical and electrical characteristics are combined[33].

The mobilities of solvated electrons, protons, and ions in certain polar liquids.

Liquid	D_{st}	T, °C	μ(H+), cm^2 V^{-1} s^{-1}	μ(m.i.), cm^2 V^{-1} s^{-1}	$\mu(e_S)$, cm^2 V^{-1} s^{-1}	η, cP	References
Water	81	20	$4\cdot10^{-3}$	$1\cdot10^{-3}$*	$2\cdot10^{-3}$	1.0	52
Methanol	31	20	$1.4\cdot10^{-3}$	$9\cdot10^{-4}$*	$2.8\cdot10^{-3}$	0.58	46,55
Hexamethyl-phosphoramide	30	20	—	$6\cdot10^{-5}$	$5.5\cdot10^{-4}$	3.6	33
Ammonia	22	−60	$1.3\cdot10^{-3}$	$1.8\cdot10^{-3}$*	$1\cdot10^{-2}$	0.37	54,56
1-Propanol	20	20	$3.6\cdot10^{-4}$	$1.8\cdot10^{-4}$	$4.6\cdot10^{-4}$	2.39	47,46
Isopropyl alcohol	19	20	$2.4\cdot10^{-4}$	$1.5\cdot10^{-4}$	$4.5\cdot10^{-4}$	3.95	47,46
Dimethoxyethane	13	−90	—	$4\cdot10^{-5}$*	$4\cdot10^{-4}$	32.3	57,58
Monobutylamine	5	20	—	$2\cdot10^{-3}$	$2.7\cdot10^{-3}$	0.35	33

*The average mobilities of alkali metal and halide ions.

Spectroscopic measurements showed that in the organic liquids investigated solvated electrons generated by high-energy electron pulses disappear via a pseudofirst-order reaction. By reacting with acceptors or matrix molecules, the electron passes from the solvated state, detected by means of the optical absorption and characterised by the lifetime $\tau = k_{opt}^{-1}$, to a bound state. This entails a change in the mobility of the charged species. Numerical values of $\mu(e_S)$ were obtained by treating the current relaxation curves in terms of the equations[33]:

$$I_{max} = FG(e_s)PS[\mu(e_s) + \mu((m.i.)]/100;$$
$$\frac{I(t)}{I_{max}} = 2\left[\frac{\mu(e_s)}{\mu(m.i.)} + 1\right]^{-1} + \left\{\frac{[\mu(e_s)/\mu(m.i.)] - 1}{[\mu(e_s)/\mu(m.i.)] + 1}\right\} e^{-k_{opt}\cdot t}, \quad (3)$$

where $G(e_S)$ is the radiation-chemical yield of solvated electrons, P the dose in the pulse, $\mu(e_S)$ and μ(m.i.) are the mobilities of solvated electrons and molecular ions, F is the electric field strength, S the area of the electrodes, and I_{max} the maximum amplitude of the relaxation current. The Table lists the mobilities of solvated electrons, protons, and ions for certain polar liquids.

The data quoted by Vannikov et al.[33] first led to the conclusion that the mobility of solvated electrons in various polar media is inversely proportional to their viscosities. Recently this conclusion was confirmed in a study[55] where it was shown that the Walden rule holds for solvated electrons, and $\mu(e_S)\eta = C$. Fig. 4 presents the known mobilities of solvated electrons as a function of the viscosity of the polar liquid. The straight line corresponds to the Walden rule with $C = 2 \times 10^{-3}$ cm^2 cP V^{-1} s^{-1}. The values of $\mu(e_S)$ are quoted for room temperature, with the exception of ammonia (−60°C) and dimethoxyethane (−90°C). Since the relation $\kappa = \mu kT/e$ holds between the mobility and the diffusion coefficient κ, one can assume that a relation analogous to that illustrated in Fig. 4 holds between $\kappa(e_S)$ and η.

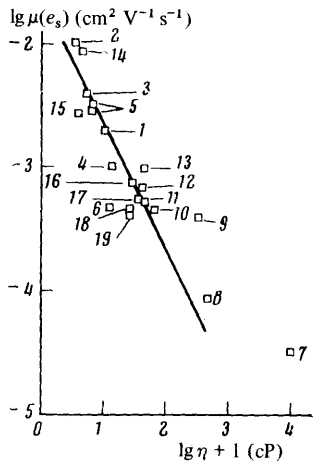

Figure 4. Variation of the mobility of the solvated electron with viscosity in polar liquids: 1) water[52]; 2) ammonia[54]; 3) n-propyl ether[55]; 4) ethanol[55]; 5) methanol[46,55]; 6) ethanol[65]; 7) glycerol[50]; the data for the remaining limits were taken from Refs. 33, 46, 47, and 57: 8) 1,2-propylene glycol; 9) dimethoxyethane; 10) hexanol; 11) 1-pentanol; 12) isobutyl alcohol; 13) isopentyl alcohol; 14) ethyl methyl ketone; 15) monobutylamine; 16) 1-butanol; 17) hexamethylphosphoramide; 18) 1-propanol; 19) isopropyl alcohol.

The results obtained for polar liquids, referring to various classes of organic compounds, show that in all cases the mobility of solvated electrons is much higher than that of molecular ions, with the exception of water, where the mobilities of electrons and hydroxide ions are the same; however, one should note that hydroxide ions exhibit anomalous mobility. Thus the mechanism of the motion of solvated electrons differs from that of the usual diffusion of ions. The activation energy for mobility measured for solvated electrons in hexamethylphosphoramide is 1.6 kcal mole^{-1} and is smaller than the activation energy for ionic mobility (4.4 kcal mole^{-1}).[59] On the other hand, the specific characteristics of the diffusion of solvated electrons distinguish it from the mechanism of the motion of protons (it has been suggested[60] that the same mechanism applies to hydrated electrons and H^+ ions), which in

certain liquids, for example in water and alcohols, leads to anomalous mobilities, since high values of $\mu(e_S)$ relative to ionic mobilities are observed also in liquids where there is no anomalous proton mobility.

In principle it is possible to postulate a mechanism for the motion of e_S based on the transition of the electron to a quasifree state with a high mobility and its subsequent solvation. Estimates based on experimental results, [19,61] have shown [46] that the minimum activation energy for the process exceeds 10 kcal mole^{-1}, which is much more than the experimental value quoted above and makes this mechanism of the motion of e_S unlikely in polar organic liquids. The jump mechanism of the motion of the electron between local regions in the liquid where orientation polarisation corresponds to a minimum in the overall electron energy appears to be more realistic [62]. The diffusional jump is accompanied by a reorientation of the liquid molecules and one may expect a correlation between the viscosity and the mobility $\mu(e_S)$, which is in fact observed, as shown above.

Thus empirical relations and gas-phase data for the interaction of electrons with organic molecules as well as macroscopic characteristics of the organic liquid and its molecular parameters make it possible to determine approximately beforehand whether solvated electrons will be formed in the given liquid and to indicate the part of the spectrum where the e_S absorption band should occur, the parameters of the spectrum, and the expected mobility and diffusion coefficient of e_S. Theoretical proof of the above characteristics will promote a significant advance in the understanding of the nature of the solvated state of electrons in polar organic liquids.

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The Intermediate Chemisorbed Species in Electrocatalysis

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The fundamental data on the adsorption of various organic substances on platinum, obtained by electrochemical methods, are discussed. It is shown that electrochemical pulse methods make it possible to determine the degree of adsorption directly under the steady-state conditions of an electrocatalytic process and also to establish in many instances the nature of the adsorbed complex on the surface of the catalyst electrode.
The bibliography includes 70 references.

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I. INTRODUCTION

In many electrochemical oxidation-reduction reactions the electrode behaves simultaneously as a catalyst on the surface of which purely catalytic processes can take place and individual stages of electrochemical processes can be accelerated. The catalytic processes which may precede the electron transfer stage and facilitate it, can follow this stage, or can proceed independently of and simultaneously with the main electrochemical process. The studies in recent years on a large number of electrochemical processes involving organic compounds have shown that the slow stage in such processes is frequently the purely catalytic reaction, while the electrochemical stage merely supplies one of the reactants.

The problem of the direct transformation of the chemical energy of fuel into electrical energy in fuel cells stimulated extensive research on the characteristics of the kinetics of electrode processes, of adsorption on solid electrodes, and of the influence of the nature and structure of the catalyst electrode on its electrochemical activity in relation to various reactions. To embrace the entire range of processes, the term "electrocatalysis" is widely used, showing clearly that these processes are on the border line between two fields of physical chemistry—electrochemistry and catalysis. In the study of the mechanisms of electrocatalytic processes, both the classical methods of heterogeneous catalysis and the electrochemical methods developed in recent years are used.

The considerable advances in electrocatalysis in recent years are due to two main achievements—the development of electrochemical methods for the investigation of the adsorption of reactants (and also of intermediates) and for the preparation of a reproducibly clean electrode surface and the determination of the degree of its purity.

Systematic research on adsorption phenomena by electrochemical methods was begun in 1933–1938 by Frumkin and his coworkers [1-3], who determined with the aid of the so called charging curves (curves relating the potential of a polarisable electrode to the amount of electricity passed through the system) not only qualitative but also quantitative aspects of the adsorption of hydrogen and oxygen on platinum and other platinum group metals. The most important results of these studies were the determination of the distribution of adsorbed species among adsorption sites with different bonding energies and the demonstration that the adsorption isotherm is logarithmic (Temkin's isotherm):

$$\theta = a + \frac{1}{f} \ln c,$$

where θ is the degree of surface coverage by the adsorbed species, c the concentration in solution (the partial pressure for gases), and a and f are constants (the constant f is sometimes called the surface inhomogeneity factor). These experimental observations served as a basis for the development of a theory of adsorption phenomena and of the kinetics of chemical reactions on a surface with uniformly distributed inhomogeneities [4,5], which had been widely used in heterogeneous catalysis. In the above experimental studies the charging curves were recorded very slowly (i.e. small currents were used), thereby ensuring a state close to equilibrium at almost all points.

In recent years electrochemical methods for the investigation of adsorption phenomena have been greatly developed. A number of new experimental procedures have been devised, whereby measurements can be made at a high rate, which admittedly infringes in many cases the equilibrium in the system, but on the other hand such rapid methods permit the determination not only of the overall degree of adsorption but also of its kinetics. Electrochemical methods have been used to study the adsorption of not only hydrogen and oxygen but also of a large group of other substances, particularly various organic compounds [6-8].

Electrochemical pulse methods make it possible to determine the degree of adsorption directly under the steady-state conditions of catalytic and electrocatalytic processes and to establish in many instances the nature of the complex adsorbed on the surface of the catalyst electrode.

II. THE DISSOCIATIVE NATURE OF THE CHEMISORPTION OF ORGANIC SUBSTANCES ON PLATINUM GROUP METALS AND THE NATURE OF THE CHEMISORBED SPECIES

From an analysis of the variation of the kinetics of the decrease of potential in the adsorption of methanol on a platinum electrode with the pH of the solution, Frumkin and Podlovchenko[9] put forward for the first time in 1963 the hypothesis that the adsorption (more correctly chemisorption) of methanol from solution on platinum is accompanied by the abstraction of hydrogen atoms from the adsorbed methanol molecule, i.e. its degradation. The use of various combined electrochemical methods and also the tracer atom method made it possible to show subsequently that, following its adsorption on the platinum electrode, the methanol molecules split off three hydrogen atoms. The resulting COH species is bound directly to three surface platinum atoms, liberating three electrons when it is oxidised to CO_2.[10] The results show that the adsorption of methanol can be represented as follows:

$$CH_3OH \rightarrow \underset{\times\times\times}{COH} + 3H_{ads},$$

where the crosses indicate the number of surface platinum atoms forming strong bonds with the adsorbed species.

On open external circuit, both hydrogen and the carbon-containing residues formed during dehydrogenation remain on the electrode surface. However, the hydrogen atoms completely lose their bonds with the carbon-containing species and are linked to the catalyst surface only. They behave as free adsorbed hydrogen atoms in equilibrium with the hydrogen ions in the bulk of the solution and determine the electrode potential. Hydrogen can diffuse to the opposite side of a palladium membrane, where it can be detected[11-14].

Using the large difference between the oxidation potentials of the adsorbed hydrogen and the carbon-containing residues, it is possible to remove the hydrogen atoms from the surface by applying to the electrode a potential $\varphi_r = 0.4$ V (φ_r is the potential relative to that of the reversible hydrogen electrode in the same solution), which is intermediate between the above two potentials; an additional amount of carbon-containing COH residues is then adsorbed on the liberated surface sites. This constitutes the main difference between adsorption under the usual catalytic conditions (on open external circuit) and under electrochemical conditions (when the circuit is closed). When the circuit is closed and the potential is maintained at values more positive than 0.3 V, the maximum degree of adsorption of the species can be almost a factor of two greater than that observed on open circuit.

This mechanism of the adsorption of methanol on platinised platinum was confirmed using methanol labelled with ^{14}C and tritium[15]. Thus in the adsorption of $^{14}CT_3OH$ on a platinised platinum electrode at a potential such that hydrogen should be removed from the electrode surface, only species containing ^{14}C are adsorbed, but the adsorbed species does not contain tritium.

Experiments showed that the nature of the chemisorbed species does not change when the electrode potential, the concentration of methanol, the pH of the solution, and temperature are altered. There is no doubt that the dehydrogenation process does not proceed immediately via the elimination of three hydrogen atoms but involves separate stages:

$$\underset{\times}{CH_3OH} \xrightarrow{k_1} \underset{\times\times}{CHOH} + H_{ads};$$

$$\underset{\times\times}{CHOH} \xrightarrow{k_2} \underset{\times\times\times}{COH} + H_{ads},$$

where $k_1 < k_2 < k_3$, so that the elimination of the first hydrogen atom is slowest, the second and third atoms being removed more rapidly.

Similar methods have been used to establish the nature of the chemisorbed species on platinum group metals in the adsorption of various organic substances (hydrocarbons ranging from methane to hexane, alcohols from methanol to octanol, formic acid, formaldehyde, carbon dioxide, ethylene glycol, glycolaldehyde, nitromethane, nitroethane, maleic acid, etc.). It has been shown that the chemisorbed species formed initially in the adsorption of organic molecules can be transformed on the surface as a result of secondary reactions into other species, more stable under the given conditions. For example, formic acid adsorbed on a platinum electrode gives rise to the primary species COOH,[16-18] i.e.

$$HCOOH \rightarrow H_{ads} + \underset{\times}{COOH},$$

which reacts at $\varphi_r < 0.4$ V with adsorbed hydrogen:

$$\underset{\times}{COOH} + 2H \rightarrow \underset{\times\times\times}{COH} + H_2O,$$

yielding the same species as in methanol solutions. Chemisorbed species resulting from the partial oxidation of the initial species can also be present on the surface. For example, in a study of the adsorption of methane on the surface of a platinum electrode it was shown that the chemisorbed species is similar to that derived from methanol, having the composition COH.[19,20]

At room temperature carbon dioxide is not usually adsorbed on the surface of a platinum electrode free from adsorbed gases, but is readily adsorbed on the surfaces of the electrode on which hydrogen has been adsorbed (i.e. as a result of reaction with hydrogen). This leads to the formation of chemisorbed species similar to that obtained in methanol solutions[21-25].

The processes occurring in the adsorption of compounds containing two and more carbon atoms in the molecule are much more complex, so that it is now difficult to determine their nature, particularly when the adsorption proceeds on open circuit and the adsorbed hydrogen remains on the surface. Cracking, hydrogenation, and polymerisation can then occur[26,27]. The mechanism of cracking, i.e. of the dissociation of the C–C bond, has been studied in detail[29-32] in the adsorption and oxidation of ethylene, ethane, and other hydrocarbons on a platinum electrode. In the adsorption of ethylene and ethane two types of chemisorbed carbon-containing species are formed—species which are oxidised readily and with difficulty. The species which are difficult to oxidise contain two carbon atoms and are readily removed from the surface by hydrogenation, forming ethane. The readily oxidised species contain one carbon atom and are hardly hydrogenated.

The mechanism of the adsorption of ethylene and ethane on platinum can be represented as follows:

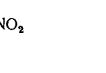
$$\begin{array}{l} CH_2{=}CH_2 \\ \quad\downarrow k_{ads} \\ CH_3{-}CH_3 \underset{+2H_{ads}}{\overset{-2H_{ads}}{\rightleftharpoons}} \underset{\times\quad\times}{CH_2{-}CH_2} \xrightarrow{k_{decomp}} \end{array}$$

[species (II)]

$$\begin{array}{l} \quad\quad CO_2 \\ \quad\quad\uparrow \\ \rightarrow \underset{\times\times}{CH_2} \rightarrow \underset{\times\times\times\times\times\times}{CH} \rightarrow \underset{\times\times\times\times\times\times}{COH} \end{array}$$

[species (I)]

The principal constants for the adsorption of various organic substances on a platinum electrode.

Substance	Electrode, solution*	φ_r, v	t, °C	Nature of chemisorbed species	θ'^{max}_R	a	f'	k_{ads}, cm s^{-1}	E^0_a, kcal $mole^{-1}$	C_α	References
1	2	3	4	5	6	7	8	9	10	11	
H_2	A	0	20	H ×	1	—	14	$2.7\cdot10^{-3}$	—		
	B	0	20	H ×	1	—	14	—	—		33–35
	A, alk	0	20	H ×	1	—	14	$3.4\cdot10^{-3}$	—		
CH_4	B	0.2	80	COH ×××	—	—	—	—	—		19, 20
CH_3OH	A	0.4	25	COH ×××	0.78	0.82	14	$1.4\cdot10^{-5}$	9.5		
	B	0.4	25	COH ×××	0.75	0.82	7.4	$2\cdot10^{-6}$	9.5		8, 10, 26, 36–43
	A, alk	0.4	25	COH, CO⁻ ××× ×××	0.7	0.65	14.4	$2.1\cdot10^{-6}$	—		
HCHO	A	0.4	25	C=O ××	0.85	1.6	—	$2.4\cdot10^{-3}$	—		
	B	<0.4	25	COH ×××	—	—	—	—	—		44, 45
HCOOH	A	0.4	41	COOH ×	0.83	0.96	15	$4.3\cdot10^{-5}$	5.2		
	A	0.2	41	COH ×××	0.83	1.22	15	$1.7\cdot10^{-3}$	—		8, 16, 17, 26, 37, 38
	B	<0.4	20	COH ×××	—	—	—	—	—		
CO_2	A	0 02	20	COH ×××	0.75	—	15	$1-2\cdot10^{-4}$	7.4		21–25
	B	<0.4	20	COH ×××	—	—	—	—	—		
CH_3NO_2	A	0.4	20		0.6	0.69	14	$7.4\cdot10^{-6}$	—		46, 47
	A	0.2	20		—	0.8	21	$4.2\cdot10^{-4}$	—		
C_2H_4	B	0.2	90	H_2CCH_2, CH_2, CH, ×× ×× ××× COH ×××	—	—	14	$7.9\cdot10^{-4}$	—		28–32
C_2H_6	B	0.2	90	H_2CCH_2, CH_2, CH, ×× ×× ××× COH ×××	—	—	14	$5.1\cdot10^{-4}$	—		28–32
C_2H_5OH	AB	0.4	25	COH, CH_3COH etc. ××× ××	0.79	0.95	14	$3.5\cdot10^{-5}$	—		26, 48, 49
$(CH_2OH)_2$	A	0.4	25	HOC——COH ××××	0.65	1.05	14	$8.7\cdot10^{-4}$	16.4		27
	A	0.4	>50	COH ×××	—	—	—	—	—		
OCH—CH_2OH	A	0.4	20	OCH—COH, OC—COH ×× × ××	0.84	1.2	13,5	$1\cdot10^{-3}$	12.8		50
HOOCCH= =CHCOOH	A	0.4	20	HOOCCH—CHCOOH × ×	0.43	1.3	14	$1.1\cdot10^{-3}$	2.3		
cis-	A	0.05	20	HOOCCH—CHCOOH × ×	0.3	0.6	16	$2.5\cdot10^{-4}$	—		51–42
trans-											
C_3H_6	B	0.2	90	C_3, CH, CH_2, COH ××× ×× ×××	—	—	14–19	$2\cdot10^{-5}$	—		53
C_3H_7OH	A	0.4	25	C_3, COH etc. ×××	0.62	0.95	14	$8\cdot10^{-6}$	—		48, 49
n-$C_5H_{11}OH$	A	0.4	25	C_5, COH etc.	0.44	0.95	14	$1\cdot10^{-5}$	—		
i-$C_5H_{11}OH$	A	0.4	25	C_5, COH etc.	0.62	0.92	14	$4.7\cdot10^{-7}$	—		48, 49
	A	0.4	25	—	0.88	1.5	11.5	$1\cdot10^{-3}$	—		54
Urea	A	2.1	25	—	0.5	0.39	13	$3.5\cdot10^{-5}$	—		55

*Electrode: A—smooth platinum; B—platinised platinum; solution: alk—alkaline (1 *N* KOH); no symbol acid (0.5–1 *N* H_2SO_4).

The relative amounts of species (II) and (I) depend on the ratio of the rate constants for adsorption and decomposition.

The experimental data available at present show that, in the adsorption of organic compounds on platinum, triple and double bonds are dissociated most readily, dehydrogenation at the α-carbon atom is more difficult, and the hydrocarbon group is dehydrogenated and C–C bonds are ruptured only under more severe conditions. With increase of temperature, the degrees of dehydrogenation and degradation of the initial molecule also increase.

The Table presents the main constants characterising the adsorption processes of certain organic substances on smooth and platinised platinum electrodes.

III. THE FUNDAMENTAL CHARACTERISTICS OF THE ADSORPTION OF ORGANIC SUBSTANCES ON PLATINUM

It has been shown in numerous investigations [8,16,27,38,56,57] that the dependence of the surface coverage of the platinum electrode θ'_R on the bulk-phase concentration of the organic substance at different potentials, temperatures, and pH values is described by Temkin's logarithmic isotherm at moderate coverages (Figs. 1 and 2):

$$\theta'_R = a + \frac{1}{f'} \ln c$$

(the degree of coverage θ'_R is defined as the ratio of the occupied sites to the number of surface sites available for

the adsorption of hydrogen; since f depends on the definition of θ, it is designated in this case by f'). The quantity a (characterising adsorbability) depends on the electrode potential, the pH of the solution, and the nature of the organic substance, while the values of f' are almost the same ($f' = 14 \pm 2$) for the adsorption of a wide variety of organic substances on platinum electrodes. The dimensions of the adsorbed species have a marked influence on the limiting surface coverage $\theta_R'^{max}$ and on the fraction of the surface blocked owing to steric hindrance.

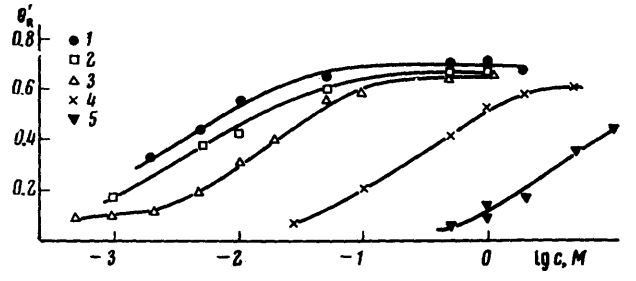


Figure 1. Steady-state methanol adsorption isotherms on a platinised platinum electrode in 1 N H_2SO_4 at various potentials φ_r (V): 1) 0.5; 2) 0.55; 3) 0.6; 4) 0.7; 5) 0.8.

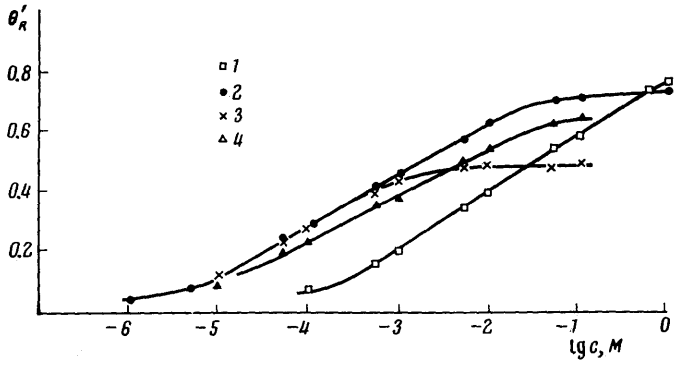


Figure 2. Steady-state isotherms for the adsorption of various aliphatic alcohols on a smooth platinum electrode in 1 N H_2SO_4 at an adsorption potential $\varphi_r = 0.4$ V: 1) CH_3OH; 2) C_2H_5OH; 3) n-$C_5H_{11}OH$; 4) t-$C_5H_{11}OH$.

The rates of adsorption on platinum of all the organic substances investigated are described under different conditions by the Roginskii–Zel'dovich equation (Figs. 3 and 4): [8,16,27,38,56-59]

$$v_{ads} = k_{ads} c \exp(-\alpha f' \theta_R'),$$

where α is the transfer coefficient (usually $\alpha \simeq 0.5$). On passing from one organic substance to another, the adsorption rate constants vary approximately in the same sequence as the adsorbabilities. The results of studies of the variation of k_{ads} with potential have shown that it is influenced mainly by the adsorption of hydrogen and oxygen which is related to the potential, and not by the electrode potential itself [8,16,26,27]. Therefore the equation for the rate of adsorption of an organic substance can be written as follows:

$$v_{ads} = (1 - \Sigma\theta_i) k_{ads} c \exp(-\alpha f' \Sigma\theta_i'),$$

where the summation is carried out over all the chemisorbed species: organic species, oxygen, hydrogen, etc.

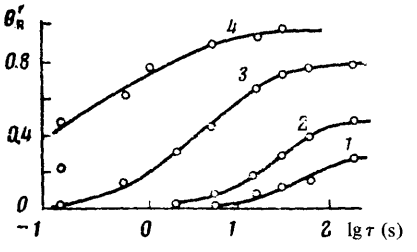


Figure 3. Kinetics of the adsorption of methanol on a smooth platinum electrode in 1 N H_2SO_4 at an adsorption potential $\varphi_r = 0.4$ V and various methanol concentrations (M): 1) 0.001; 2) 0.01; 3) 0.1; 4) 1.

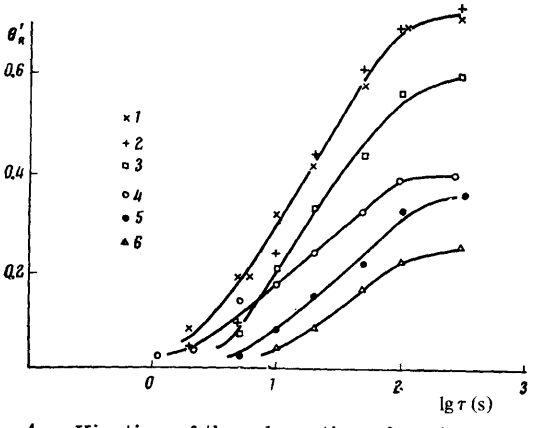


Figure 4. Kinetics of the adsorption of various organic substances on a platinum electrode at a potential $\varphi_r = 0.4$ V: 1) saturated ethylene solution in 1 N KOH; 2) saturated ethylene solution; 3) 10^{-4} M allyl alcohol; 4) 10^{-4} M maleic acid; 5) saturated styrene solution diluted 100 times; 6) 10^{-4} M furmaric acid; 2) 1 N H_2SO_4.

The activation energies E_a for the adsorption of various organic substances on platinum increase linearly with surface coverage (Fig. 5): [16,27,50,57]

$$E_a = E_a^0 + \alpha f' R T \theta_R'.$$

The observed kinetic and adsorption characteristics permitted a quantitative interpretation of the nature of the curves describing the decrease of the electrode potential on open circuit when an organic substance is introduced into the solution [60,61].

The kinetics of the elimination of chemisorbed species from the surface of platinum (Fig. 6) are described by the equation

$$v_{sp.} = k_{sp.} \exp(\beta f' \theta'_R),$$

where β is the transfer coefficient (usually $\beta \simeq 0.5$). Chemisorbed nitromethane, nitrobenzene, acetic acid, and maleic acid species are removed as a result of their hydrogenation [47,51] and methanol species are removed as a result of oxidation.

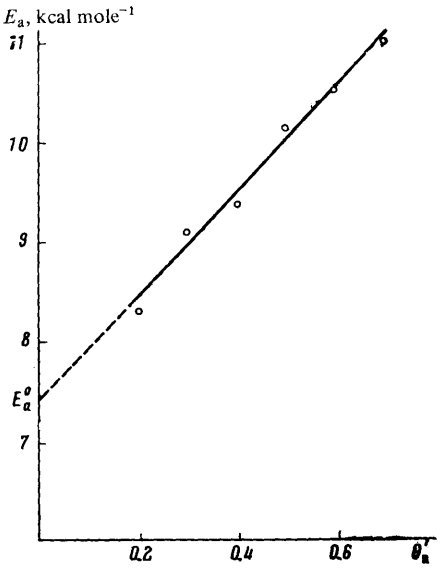


Figure 5. Variation of the activation energy E_a with θ'_R in the adsorption of CO_2 in 1 N H_2SO_4 at a potential φ_r = 0.1 V and p_{CO_2} = 1 atm.

Determination of the variation of the heat of adsorption of methanol on a platinum electrode with surface coverage showed that the applicability of Temkin's logarithmic isotherm to adsorption is a result of a linear relation between the heat of adsorption Q_{ads} of methanol and surface coverage [57]:

$$Q_{ads} = Q^0_{ads} - f' R T \theta'_R.$$

IV. DEPENDENCE OF THE ADSORPTION OF ORGANIC SUBSTANCES ON THE POTENTIAL

The dependence of the adsorption of neutral organic substances on the potential for mercury and many other metallic electrodes is determined primarily by the position of the zero-charge point and the electrostatic effect of the charges of the electrical double layer [62,63]. Frumkin showed by a thermodynamic procedure [64,65] that a different situation should obtain for platinum and certain other electrodes capable of adsorbing large amounts of hydrogen and oxygen. When the adsorption process is reversible, the degree of adsorption of the organic substance should decrease even for low degrees of surface coverage by hydrogen or oxygen; the maximum degree of adsorption of the organic substance may be expected in the range of potentials between the regions corresponding to the adsorption of hydrogen and oxygen.

Experiment has shown that the variation of the degrees of adsorption of many organic substances on platinum with the potential is normally described by a dome-shaped curve with a broad maximum in the potential range 0.3 to 0.6 V, where the degree of adsorption of hydrogen and oxygen are minimal (Figs. 7 and 8). [5,8,17,38,66] The constancy of surface coverage in this range of potentials shows that the potential itself on the charge of the double layer hardly affects the adsorption of methanol, since the specific adsorption forces are much greater than the electrostatic influence of the surface charge.

When the potential shifts towards more negative ($\varphi_r <$ 0.3 V) or more positive ($\varphi_r \geq$ 0.5–0.6 V) values, the

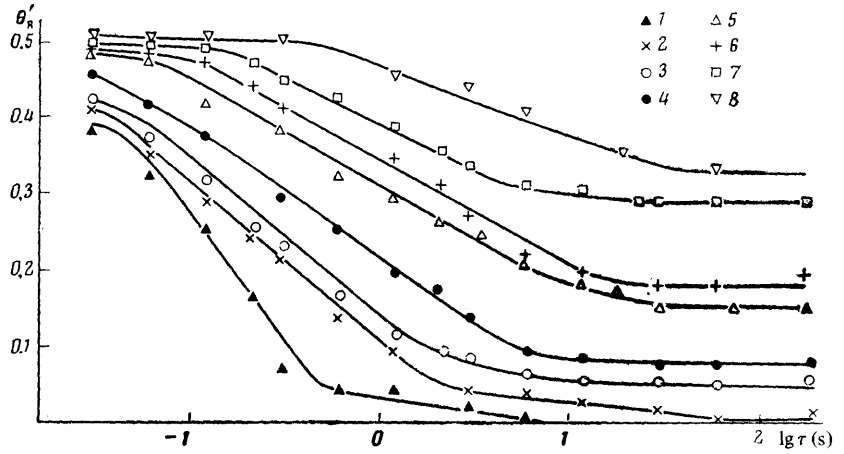


Figure 6. Kinetics of the hydrogenation of species chemisorbed at φ_r = 0.2 V from 10^{-4} M $C_4H_4O_4$ + 1 M H_2SO_4 solutions at various hydrogenation potentials (V): 1) −0.025; 2) 0.0; 3) 0.0125; 4) 0.025; 5) 0.05; 6) 0.075; 7) 0.1; 8) 0.125.

degree of adsorption falls (to a first approximation linearly as the potential is altered). The decrease of the degree of adsorption at negative potentials is due to the influence of the adsorption of hydrogen on the adsorption of the organic residue or to the hydrogenation of the species.

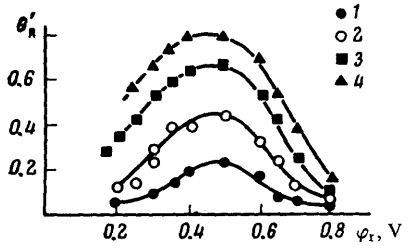


Figure 7. Variation of θ'_R with the potential φ_r in the adsorption of methanol on a smooth platinum electrode in 1 *N* H_2SO_4 solutions for different methanol concentrations (M): 1) 0.001; 2) 0.01; 3) 0.1; 4) 1.

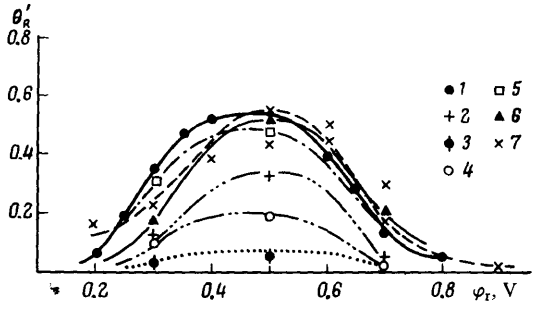


Figure 8. Variation of θ'_R with the potential φ_r on a smooth platinum electrode for 0.01 M methanol in 1 M phosphate buffer solutions at different pH: 1) 0.32; 2) 1.4; 3) 2.8; 4) 6.2; 5) 10.1; 6) 12.2; 7) 13.1.

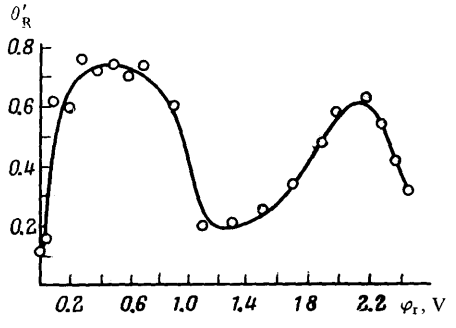


Figure 9. Variation of θ'_R with the potential φ_r in 1 *N* H_2SO_4 + 10^{-3} M C_4H_6 solution.

The decrease of surface coverage at positive potentials is associated with the oxidation of the chemisorbed species, since the rates of adsorption and electrochemical oxidation become comparable. The width and position of the dome-shaped curve for different organic substances may vary somewhat owing to the changes in the relative rates of individual processes (adsorption, oxidation, hydrogenation, etc.).

Experiment shows that, to a first approximation, the curve relating the degree of adsorption of the organic substance to the potential shifts with pH in the same way as the hydrogen and oxygen adsorption regions [8,47,51]. The shift of the adsorption regions of the organic substances as the pH of the solution is varied constitutes a characteristic property of the platinum electrode and of other electrodes adsorbing considerable amounts of hydrogen.

It has been shown for the adsorption of butadiene [54] and urea [55] on platinum that at high anodic potentials the organic substance can be adsorbed on an oxide layer, which leads to the appearance of a second adsorption maximum at $\varphi_r = 2.2$ V (Fig. 9).

V. THE INTERMEDIATE CHEMISORBED SPECIES AND THE MECHANISMS OF ELECTROCATALYTIC PROCESSES

The influence of pH and electrode potential on the rates of electrochemical oxidation [67-70] and electrochemical reduction [46-51] of various organic substances on platinum group metals shows that, apart from the adsorbed organic species, another species, formed in the preceding rapid electrochemical stage is involved in the slow stage. In an oxidation reaction the adsorbed species is OH_{ads}, formed as a result of the electrochemical oxidation of water:

$$H_2O \rightleftarrows OH_{ads} + H^+ + e.$$

The slow stage in the oxidation of methanol is the non-electrochemical interaction of carbon-containing chemisorbed species with OH_{ads} radicals. In acid solutions the slow stage is

$$\underset{\times\times\times}{C} - OH + OH_{ads} \rightarrow \underset{\times\times}{C}{=}O + H_2O;$$

the subsequent oxidation stages being faster. Similarly the slow stages in the oxidation of formaldehyde and formic acid are the reactions

$$\underset{\times\times}{C}{=}O + OH_{ads} \rightarrow \underset{\times}{C}\begin{matrix}{=}O\\ \diagdown OH\end{matrix};$$

$$\underset{\times}{C}\begin{matrix}{=}O\\ \diagdown OH\end{matrix} + OH_{ads} \rightarrow CO_2 + H_2O.$$

Under steady-state electrochemical oxidation conditions, methanol is dehydrogenated and OH_{ads} radicals are formed simultaneously. Bearing in mind that the dehydrogenation of methanol does not proceed in a single stage via the abstraction of three hydrogen atoms but involves a series of stages, presumably the OH radicals formed react with methanol at any stage in its dehydrogenation, giving rise to various oxidation products. Therefore the entire oxidation process can be represented schematically as shown in Fig. 10.

Detailed studies of the mechanism of the adsorption and electrochemical oxidation of simple organic substances ranging from methane to carbon dioxide on platinum group metals have shown that, despite the great complexity and wide variety of these reactions, they can be described by a single multistage mechanism. The nature of the chemisorbed species on the surface is determined by the relative

rates of the individual stages in the processes, illustrated in the scheme, and also by the simultaneous electrochemical formation of the chemisorbed species OH_{ads} or H_{ads}. In its turn it determines the nature of the oxidation products under steady-state conditions. For example, at low pressures, where the conversion of species (II) into species (I) is fairly rapid, ethane and ethylene are oxidised fairly rapidly and completely to CO_2. On the other hand, at fairly high ethylene pressures, where the main chemisorbed species is H_2C-CH_2, ethylene undergoes mild oxidation to ethylene glycol.

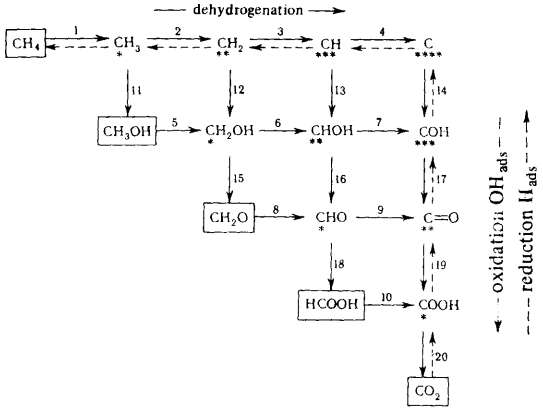
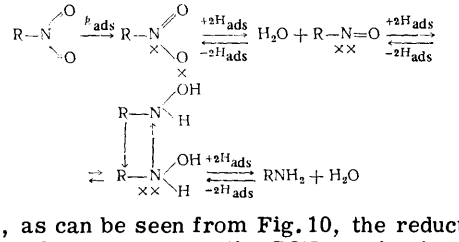


Figure 10. General scheme for the adsorption, electrochemical oxidation, and electrochemical reduction of simple organic substances.

The mechanism of the reduction of compounds with a C=C double bond has been studied in the electrochemical hydrogenation of maleic acid on a platinum catalyst electrode[51]. It has been shown that the slow stage in this process involves the interaction of the chemisorbed organic species with the adsorbed hydrogen formed in the preceding rapid electrochemical stage:

$$HOOCCH{\underset{\times}{-}}CHCOOH+2H_{ads} \rightarrow HOOCCH_2-CH_2COOH.$$

In contrast to this, in the electrochemical reduction of aliphatic nitro-compounds on platinum group metal catalyst electrodes the addition of the first hydrogen atoms is fast and the slow stage involves the addition of subsequent hydrogen atoms, which leads to the desorption of the chemisorbed organic species from the electrode surface[47]. Under these conditions, in the electrochemical reduction of nitro-compounds the surface is covered by partly reduced chemisorbed species. The overall process mechanism can be represented as follows:



Similarly, as can be seen from Fig. 10, the reduction of CO_2 by adsorbed hydrogen to the COH species is rapid and the slow stage is the subsequent interaction of this species with adsorbed hydrogen to form methane.

Thus chemisorbed species play a very important role in electrocatalytic processes, determining the direction of the process, its rate, and the yields of various products.

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The Estance Method

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A method based on the measurements of estance—the derivative of the surface tension of a conducting solid with respect to an electrical variable—is proposed for the investigation of surface phenomena. The basis of the method involves two mutually opposed effects—the change in the surface tension of the solid when its potential relative to a flowing medium is altered and the change in the potential on elastic deformation of the solid. The experimental technique, certain problems of the theory of the method, and examples of its employment are described.
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I. INTRODUCTION

The dependence of the interfacial tension between two liquids on the potential jump at the interface is known as the phenomenon of electrocapillarity[1]. As a result of research by Frumkin and his school[2-4], this phenomenon has become one of the principal sources of information about the structure of the electrode–electrolyte boundary. The large volume of information obtained by measuring the surface tensions of liquid electrodes stimulated the search for a method which would permit the measurement of the influence of the potential on the surface tensions of solid electrodes too.

II. THE SURFACE TENSIONS OF SOLID ELECTRODES

1. Principle of the Method

The variation of the surface tensions of solid electrodes with potential could not be measured previously because of the extremely slight deformation of the solid electrode and the appreciable side effects. An increase of the surface tension by 1 dyn cm^{-1} shortens a silver plate 1 cm long and 0.1 cm thick only by 0.001 Å. Appreciable internal stresses within the material of the electrode arise owing to the diffusion of extraneous species into the bulk of the electrode. Under the conditions of the example quoted, the result of the measurements may be distorted when the temperature of the electrode changes by only 10^{-6} K. In the method proposed these difficulties have been eliminated.

The essence of the method can be described briefly as follows[5-11]. If the surface tension of the solid electrode γ depends in some way on the electrode potential φ relative to the solution, then the oscillations in φ with an amplitude $\Delta\varphi$ should lead to oscillations in the surface tension with an amplitude $\Delta\gamma$. The variation of $\Delta\gamma$ with φ is recorded, the following procedure being used. The solid electrode, for example an L-shaped electrode, is clamped in a specified manner to a piezoelectric element (Fig. 1) and forms with the latter a mechanical system possessing a series of resonance frequencies. These frequencies are used in the measurements. The length of the working section of the L-shaped electrode is about 1 cm. The lower surface of the electrode is wetted by the electrolyte. It is raised somewhat above the level of the electrolyte, which makes it possible to refer to it as a suprameniscus electrode. An alternating current at a specified frequency is passed through the electrode and the potential oscillations received from the piezoelectric element are amplified at the same frequency. After rectification, this signal is applied to the vertically deflecting plates of a cathode ray tube. The horizontal scan of the beam is proportional to the average electrode potential.

Measurements can be made under two sets of conditions depending on whether one keeps constant the amplitude of the electrode charge density q (by specifying the alternating current amplitude) or the amplitude of the electrode potential φ. Under the first set of conditions, $\Delta\gamma$ is proportional to the derivative $\partial\gamma/\partial q$ and under the second set to $\partial\gamma/\partial\varphi$, which we call respectively the q-estance and the φ-estance or simply the estance (when there is no possibility of a misunderstanding). The term "estance" is modelled on the term "impedance" using as a basis the word "elastic" in connection with the study of elastic materials. The variables $\partial\gamma/\partial q$ and φ have definite advantages over others, since both these quantities have the same dimensions. They are used in the oscillograms in Figs. 2–5, where the modulus of estance $|\partial\gamma/\partial q|$, abbreviated to $|\gamma_q|$ is plotted against φ, expressed relative to the potential of the normal hydrogen electrode.

The introduction of the quantity $\partial\gamma/\partial q$ also follows naturally from a number of observed phenomena. One of these is the independence of the estance $\partial\gamma/\partial q$ of frequency in slow localised adsorption of charged species (Fig. 2*a*, on the right). This striking feature cannot be obtained by plotting $\partial\gamma/\partial\varphi$ or γ against φ.

The loss of information due to the differentiation of the $\gamma-\varphi$ relation in the process described is small. Static measurements, where there is no differentiation, nevertheless cannot yield the absolute value of γ. It is measured to within an arbitrary constant, which disappears on differentiation.

Yet another problem is important. In principle, static measurements can yield the variation of γ not only with φ

but also with the chemical potential μ of the adsorbed substance. The derivative $\partial\gamma/\partial\mu$ contains information about the concentration of this substance on the surface. However, $\partial\gamma/\partial\varphi$ can also be measured at different values of μ.

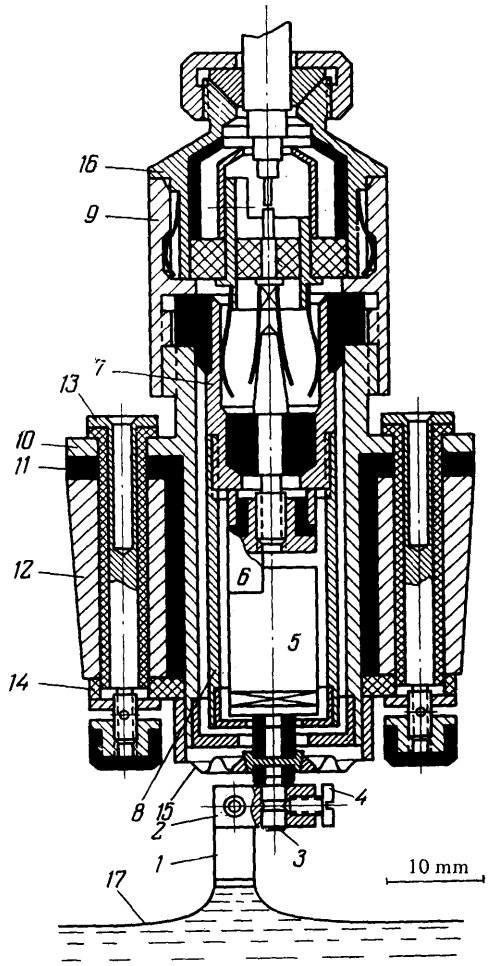

Figure 1. Unit for the transformation of surface tension: 1) L-shaped supramenisscus electrode; 2) holder; 3) shaft; 4) focussing screw; 5) piezoelectric element; 6) bush; 7) cartridge; 8) inner screen; 9) lock nut; 10) outer screen; 11) insulating beaker; 12) ground collar; 13) terminals; 14) insulating ring; 15) protective membrane; 16) coaxial plug; 17) electrolyte.

By integrating the derivative $\partial^2\gamma/\partial\mu\partial\varphi$ obtained in this way with respect to φ and starting with the desorption region (the potential φ_d at which there is no adsorbate on the electrode surface), we arrive at the following expression for $\partial\gamma/\partial\mu$:

$$\frac{\partial\gamma}{\partial\mu} = \int_{\varphi_d}^{\varphi} \frac{\partial}{\partial\mu}\left(\frac{\partial\gamma}{\partial\varphi}\right) d\varphi. \qquad (1)$$

Vanishingly small deformations of the solid electrode as a whole, occurring in measurements of the surface tension, have the same physical significance as the appreciable deformations caused by large forces. However, our aim was not to observe such vanishingly small deformations but to measure the forces under conditions where the deformations due to these forces are virtually absent.

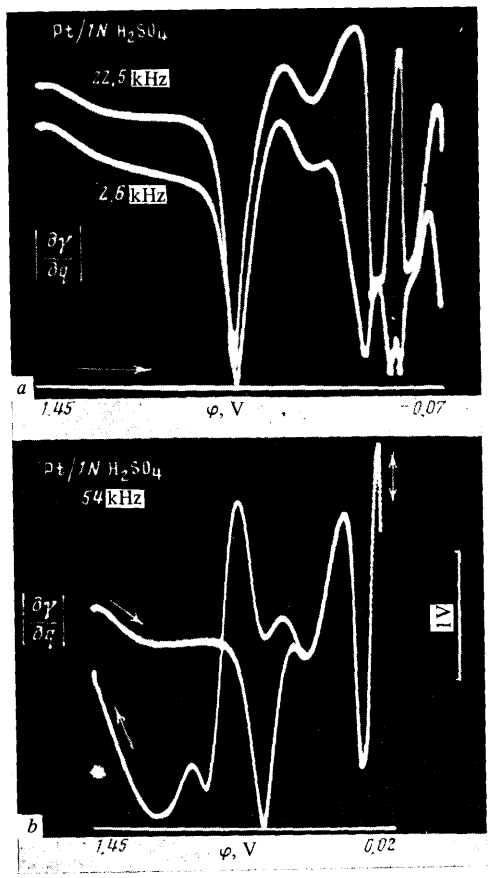

Figure 2. Estance–potential oscillograms for platinum in sulphuric acid: *a*) curves obtained by a single scan at two frequencies simultaneously; *b*) the merging of the forward and reverse curves in the hydrogen potential range

The measurements were made by comparing the surface tension with an independent standard tension, which is applied to the same surface and therefore simulates exactly the required quantity. The deformation does not have to be measured. As a result of this, the estance method is not restricted to any special shape of the electrode or to any specific mode of vibration of the electrode at different frequencies. The abandonment of deformation as the object of measurement is also natural because, when appreciable inertial forces act on the electrode, the deformation cannot serve as a unique measure of the surface tension forces.

The requirement of a small deformation is significant in the measurement of oscillating surface tensions of solids under equilibrium conditions and even more so under non-equilibrium conditions. This is because of the

influence of elastic deformation on the state of the solid and of its surface. The process of measurement can distort the surface tension if the latter is able to execute a large amount of work in altering the surface.

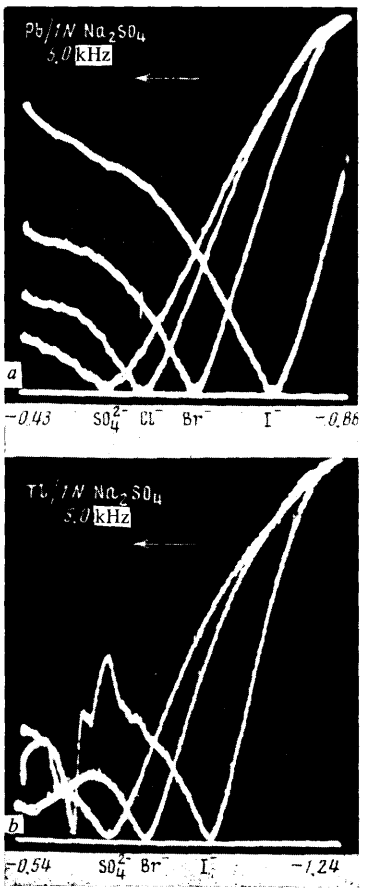

Figure 3. The influence of surface-active anions on the position of the zero estance point; electrodes: *a*) lead; *b*) thallium.

The estance method ensures a sensitivity to within not more than 0.01 dyn cm^{-1} with respect to the oscillating surface tension. It is more than enough to record exactly all the details of the dependence of the surface tension of the solid electrode on the potential. At the same time there is a capacity for a further improvement of sensitivity.

2. Experimental Technique

The results of estance measurements do not depend on the shape of the electrode. In the first experiments the electrode employed consisted of a strip of foil, which had been stretched beforehand, immersed vertically in a liquid electrolyte[5,6]. The lower end of the strip was attached to the bottom of the vessel and the upper end to a piezoelectric element built into the shell of the apparatus. With increase of the surface tension of the strip, the force applied to the piezoelectric element changes. The greater the rigidity of the piezoelectric element the smaller the shortening of the strip and the more complete the transmission of the increment in surface tension to the piezoelectric element. Thus, in measuring the force it is necessary to reduce the deformation. This constitutes the fundamental difference between the measurements of the force and deformation. The former can be achieved in general without altering the dimensions of the specimen; for this purpose, it is sufficient to balance the measured force by another force. Thermodynamically this is the most correct method of measurement. Under the given conditions, the balancing force is provided by the response of the piezoelectric element (if its rigidity is much greater than that of the foil). This device is suitable for measurements both under oscillatory and quasistatic conditions when the curve relating γ to φ is recorded directly for a linear variation of the electrode potential[5].

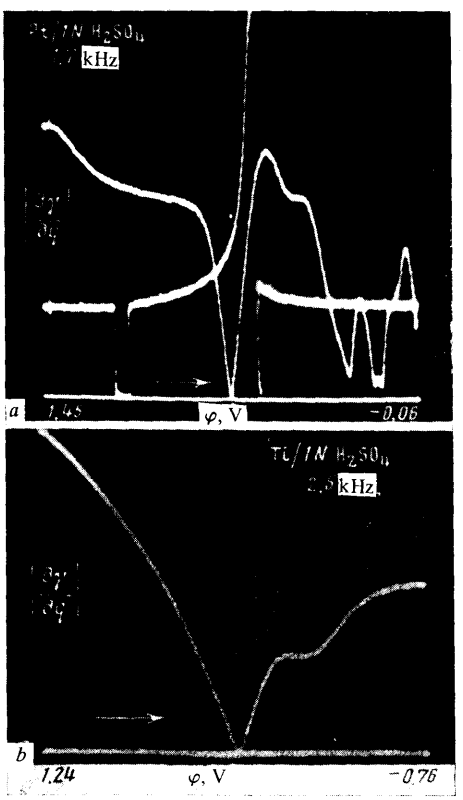

Figure 4. Estance–potential oscillograms: *a*) platinum, scale determined by thermal simulation; *b*) titanium, stepwise variation of estance in the hydrogen potential range.

Subsequently it was found that short (1 cm) and relatively thick (about 1 mm) plates can be used as the electrodes. One end of such an electrode is attached to the piezoelectric element and the other is free and immersed

in the electrolyte[8]. The piezoelectric element records the inertial force of the plate oscillating under the influence of the variable surface tension. The response of the thick (and therefore rigid) plate to the shrinking tendency of its surface layer constitutes the balancing force under these conditions. With increase of the thickness of the plate, its deformation diminishes. However, as in the previous case, the residual capacity for the improvement of sensitivity is great. Furthermore, the mass of the plate increases with its thickness, which partly compensates the loss of inertial force caused by the decrease of deformation.

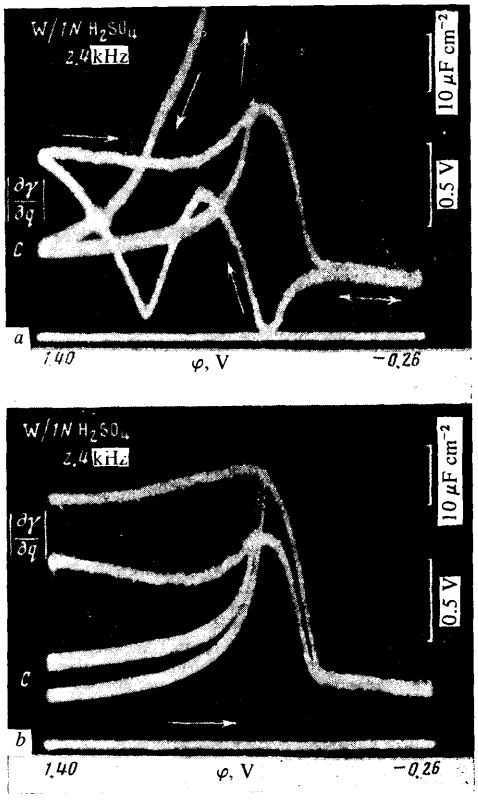

Figure 5. The variation of the estance $|\partial\gamma/\partial q|$ and the capacitance C recorded simultaneously as a function of the potential for tungsten in sulphuric acid: *a*) forward and reverse curves; *b*) different degrees of oxidation of tungsten.

A fully immersed electrode (foil strip), with both its sides operative to the same extent, was used in the first experiments because of the necessity to prevent possible distortions caused by pressure at right angles to the electrode during the passage of the alternating current[5-7]. The magnitude of this pressure was not known previously. In the course of the investigation it was found that, under the conditions of estance measurements, the above pressure is negligibly small (we shall return to its estimation at the end of this review). This made it possible to employ also electrodes with only one side operative. An example is provided by the supramenisscus electrode.

Other types of electrodes were also proposed for studies of this kind[9], for example a dipolar electrode consisting of parallel plates with the electrolyte in the gap between them and an electrode with a vertical meniscus and a non-wettable frame.

3. The Influence of Side Effects

An interesting feature of the method described is virtually complete absence of an influence by side effects, as a result of which the oscillograms recorded are identical with the estance–potential curves and do not require a preliminary treatment. The internal stresses within the bulk of the electrode are isolated because diffusion in the solid is unable to follow the oscillations of the potential jump on its surface. The Joule heating of the electrolyte is quadratic in terms of the current and varies at twice the alternating current frequency, so that it is not recorded at the frequency of the estance measurement.

The shift of the electrolyte meniscus relative to the solid electrode, caused by the effect of the potential on the wetting angle[12], is slow at frequencies in excess of 10 Hz. Insulation of the electrode at the level of the meniscus (coating of the lateral faces of the supramenisscus electrode with glass, insulation of straight plates and foil strips at the sites where they emerge from the solution) does not influence the results of estance measurements in the above frequency range. Consequently such insulation is not necessary in the experiments under consideration.

4. The Standard Tension

For polarisable electrodes, which are the main object of study in the investigation of the structure of the interfacial layer, the alternating current is consumed in charging the sides of this layer, which leads to a change in surface tension. The evolution of heat on the surface of the electrode is then negligibly small.

On the other hand, in a concentrated oxidation-reduction system at moderate frequencies the alternating current is almost wholly consumed in the electrochemical reaction which is accompanied by the evolution of an appreciable amount of Peltier heat (of the order of 0.1 cal C^{-1}). On the other hand, the interfacial layer and the surface tension hardly change under these conditions. Depending on the direction of the current, the heat of reaction is evolved or absorbed at the electrode–solution boundary. Variable thermal and mechanical stresses, which induce oscillations in the electrode plate of exactly the same type as in the oscillating surface tension at the same frequency, develop in the electrode near this boundary. It is therefore sufficient to record the readings of the apparatus in the experiment with the oxidation-reduction system to be able to assess its sensitivity to surface tension[9].

The estance–potential curve for platinum in sulphuric acid is superimposed in Fig. 4*a* on the curve for the thermal vibrations of the same platinum electrode after the replacement of sulphuric acid by a solution of the 0.2 M $K_3Fe(CN)_6$–0.2 M $K_4Fe(CN)_6$ oxidation-reduction system with a Peltier coefficient $\Pi = 0.43$ V at 20°C. Exact formulae for thermal calibration, taking into account thermal waves in the bulk of the electrode, have been published[11]. It is interesting that for platinum the coefficient in these formulae is found to be close to unity, so that the level of the horizontal section of the calibration

curve on the left-hand side of Fig. 4*a* approximately corresponds to $\Pi = 0.43$ V (we may note that the estance $\partial\gamma/\partial q$, plotted along the ordinate axis, is also measured in volts).

In order to calibrate in this way electrodes made of other metals, after the main experiments they were coated with a thin layer of gold (0.5 μm) in an electroplating bath, which protects them from disintegration in the above oxidation-reduction medium.

The heat evolved in the reversible electrochemical dissolution of the electrode itself in a specially selected medium can be employed similarly. In another method of thermal simulation of surface tension, use is made of the Peltier heat evolved at the boundary between two metals. The end of a narrow strip of platinum foil is lightly welded to the rear side of the suprameniscus electrode. For calibration, an alternating current is passed through this junction. The simulation effect is the same as for evolution of heat on the working electrode surface. This method permits calibration in the course of the main experiment. A simplification is introduced by replacing the welded foil by a drop of liquid metal (gallium or mercury). The drop is placed on the rear surface of the electrode and is connected to the current generator via a rigid conductor. If the junction between the two metals occupies an insignificant proportion of the rear electrode surface, the nature of the distribution of current in this junction is immaterial.

Another procedure for the thermal simulation of surface tension involves the passage of a high-frequency amplitude-modulated current. The surface of the electrode is periodically heated by the Joule heat evolved in the electrolyte. This operation is performed during the main experiment without changing the solution. However, it is necessary to take precautions in order to eliminate the influence of the thermal expansion of the electrolyte; in dilute aqueous solutions this can be achieved, for example, by making measurements near 4 °C (when a surface source of heat such as the heat of reaction, is employed, the bulk of the electrolyte is not heated and this precaution is of course unnecessary).

For rectangular high-frequency sinusoidal current pulses with a tracking frequency $\omega/2\pi$ and the reciprocal of the Q-factor π/α, the amplitude of the standard thermal tension at the frequency $\omega/2\pi$ is

$$\Delta\gamma_r = \frac{\sin\alpha}{\pi}\Delta j^2 r D_T^{1/2}\omega^{-3/2}\cdot\frac{1}{1-\nu}\cdot\frac{\varkappa Y}{\zeta\rho}|M|, \qquad (2)$$

where Δj is the amplitude of the current density; parameters of the electrolyte: r is the resistivity and D_T the thermal diffusivity; parameters of the electrode: ν is the Poisson coefficient, Y the modulus of elasticity, κ the coefficient of linear thermal expansion, ζ the specific heat, and ρ the density; the quantity M takes into account the loss of heat from the electrode surface; in the upper part of the audiofrequency range $|M|$ is usually close to unity; the formula for M has been published[11].

5. Thermal Tension in Adsorption on the Electrode

Apart from its main purpose, the estance method can be used also to estimate the heat evolved on the electrode during adsorption, which was apparently difficult to achieve by other methods in earlier investigations. In those rare cases where the thermal and surface tensions act simultaneously, they can be readily separated by virtue of the phase difference caused by the loss of heat to the bulk of the electrode[11]. Measurements have shown that the heat evolved in adsorption is usually negligibly small against the background of the estance values. Thus, according to an estimate made by the estance method, the evolution of heat in the adsorption reaction $H^+ + e \rightleftharpoons H_{ads}$ on platinum does not exceed 1 kcal faraday^{-1} or 0.05 V.

6. Examples of the Interpretation of the Oscillograms

Fig. 6 illustrates the estance–potential curves for platinum in sulphuric acid obtained simultaneously at frequencies of 2.6 and 22.5 kHz (they correspond to the oscillograms in Fig. 1*a* adjusted to the same vertical scale). A study was made of the range of potentials in which hydrogen is adsorbed on platinum. Therefore all the details of these curves are associated with the characteristics of the adsorption of hydrogen.

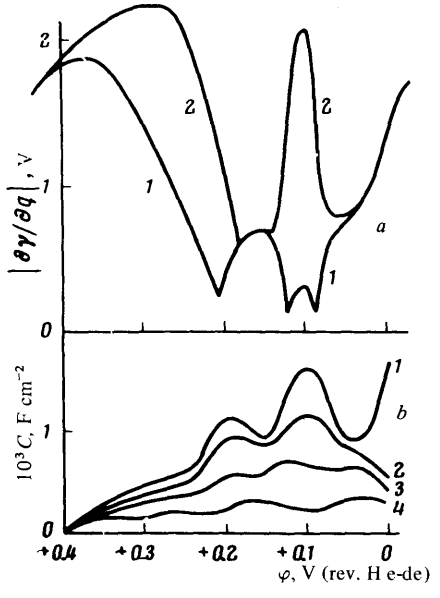

Figure 6. The influence of frequency on the variation of the estance (*a*) and the capacitance (*b*) with potential for platinum in sulphuric acid; frequency (kHz): *a*) [1) 2.6; 2) 22.5]; *b*) [1) 0.03; 2) 1.7; 3) 4; 4) 10].

The influence of frequency on estance is unexpected; sections corresponding to a strong dependence of estance on frequency alternate along the potential axis with sections where estance is almost independent of frequency and two such sections are located within the region corresponding to the adsorption of hydrogen. As the potential shifts in the cathodic direction, the sections alternate as follows: (1) from +0.50 to +0.30 V—the section where the potential is independent of frequency due to the absence of hydrogen from the platinum surface (the adsorption of hydrogen begins near +0.30 A); (2) from +0.30 to +0.18 V—the section of a strong dependence on frequency; (3) from +0.18 to +0.14 V—the section with potentials independent of frequency; (4) from +0.14 to +0.04 V—the

section of a strong dependence on frequency (there is a dip in the curve at 2.6 kHz and a peak at 22.5 kHz); (5) below +0.04 V—the section where the potential is independent of frequency [13].

For comparison, Fig. 6*b* presents the known capacitance curves for the same system at different frequencies [14]. In contrast to estance, the capacitance decreases monotonically with frequency at all the potentials in the hydrogen adsorption region. Under these conditions, the capacitance is almost wholly due to the discharge of hydrogen ions from the electrolyte before their adsorption on platinum in the form of atoms. The discharge stage is slow [3] regardless of the final state of the adsorbed atom. At high frequencies the discharge lags behind the change in periodic component of the potential, which leads to a decrease of the capacitance with frequency.

In contrast to this, the variation of estance with frequency is directly related to the *final* state of the adsorbed hydrogen atoms. It has no bearing on the discharge stage and its rate, since in the estance method the current amplitude and hence the number of hydrogen atoms which reached the surface *after* the discharge are specified beforehand. Thus the sections where estance is and is not independent of frequency separate along the potential axis adsorption regions with different final states of the hydrogen atoms.

This quite definite result follows immediately from the estance–potential oscillograms without any need for their quantitative interpretation. Another problem, i.e. the problem of the adsorption mechanisms along each of the differentiated sections, requires special study, which has been carried out [13]. Here we shall enumerate some of the results obtained here. It had been known previously that hydrogen can exist on platinum in two states (which shall be designated conventionally by H_e and H_m), but the limits of the regions corresponding to adsorption in these states had not been known. It was assumed that H_e is adsorbed initially and then H_m. It follows from the estance data that along the sections where estance is independent of frequency H_e is adsorbed (the third and fifth sections), while in the intermediate region with a strong dependence of estance on frequency H_m is adsorbed (the fourth section). Along this section, the dip in the estance curve at 2.6 kHz is due to an interruption in the adsorption of H_e and the estance peak at 22.5 kHz is caused by the internal transition $H_e \rightleftharpoons H_m$ when the potential is altered. The fact that the internal transition influences the estance markedly and is not manifested in the capacitance measurement is due to the difference between force (estance method) and energy (capacitance method). A large change in the force can be caused by an arbitrarily small energy. In this case an appreciable alteration of the surface tension is caused by a small expenditure of energy in changing the state of the interfacial layer. This is the reason for the enhanced sensitivity of the estance method to a number of processes which cannot be detected by "energy" methods.

Some of the effects detected by the estance method in the adsorption of hydrogen on platinum are illustrated in Fig. 7, which represents schematically the surface layer of platinum.

Effect of the interruption of adsorption. As the potential varies in the cathodic direction, the adsorption of external hydrogen (H_e) is interrupted by the adsorption of internal hydrogen (H_m), but begins anew after vacancies in the internal hydrogen have been largely filled.

Effect of the internal transition. There is a discrete change in the state of adsorbed hydrogen when the potential is altered. In a pure form the effect is observed at high frequencies when the supply of hydrogen from the electrolyte ceases and the overall amount of adsorbed hydrogen does not vary with potential. The transition is possible at potentials where the vacancies in both external and internal hydrogen are far from being completely filled.

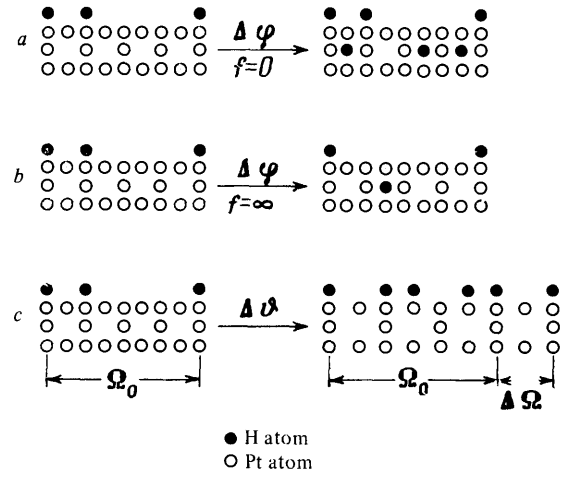

Figure 7. Schematic illustration of the effects observed by the estance method in the adsorption of hydrogen on platinum: *a*) the interrupted adsorption effect; *b*) the internal transition effect; *c*) the effect involving an increase of the surface density of adsorbed hydrogen on elastic extension of platinum; Ω_0 = initial area of the electrode; f = frequency.

Effect of the increase of adsorbed hydrogen density during elastic extension of platinum. The number of surface platinum atoms and the number of adsorbed atoms per unit surface area vary in opposite directions. With increase of the distance between the surface platinum atoms, the average distance between the hydrogen atoms diminishes. This shows that, as the platinum atoms move apart, their affinity for external atomic hydrogen rises.

The first two effects are caused by the change in electrode potential and the third is due only to the elastic deformation at a constant potential. Thus information about the events on the electrode when the potential is varied under conditions without deformation can also be obtained with equal success from the same estance–potential oscillogram.

The dual nature of estance–potential oscillograms will be considered further.

III. ELASTIC CHARGING OF THE INTERFACIAL LAYER

1. The Change in the Potential of the Polarisable Electrode on Elastic Deformation

An electrode in the form of a stretched foil strip immersed in the electrolyte undergoes periodic elastic extension and contraction with an elongation amplitude of the order of 10^{-6} at a definite frequency to which the measuring apparatus is tuned. Under the conditions of a constant charge, the potential of this electrode oscillates with an amplitude of the order of 1 μV. For a specified relative deformation amplitude, the potential oscillations are independent of the dimensions of the electrode. The results are recorded oscillographically in terms of a plot of $|\partial\varphi/\partial\theta|$ against φ, where $\theta = \Delta\Omega/\Omega$ is the relative change in the area of the electrode Ω on elastic deformation.

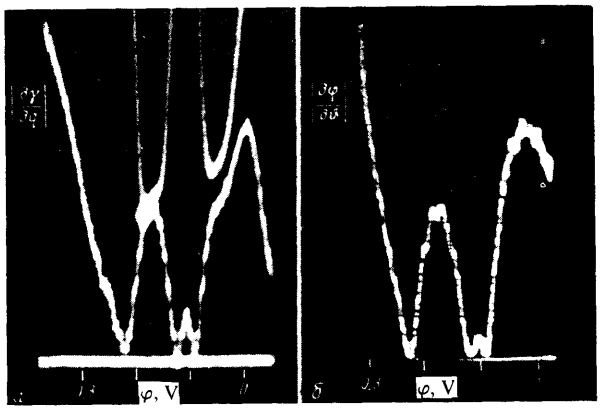

Figure 8. Comparison of oscillograms for estance (*a*) and the elastic charging of the interfacial layer (*b*); the potential is given relative to that of the reversible hydrogen electrode.

2. Mutually Opposed Effects

The $|\partial\varphi/\partial\theta|-\varphi$ oscillogram obtained in a reversible system (for example for platinum in 1 N sulphuric acid solution in the hydrogen potential range) is of exactly the same form as the $|\partial\gamma/\partial q|-\varphi$ oscillogram (Fig. 8). The significance of this agreement, which appeared unexpected in the very first experiment on elastic charging, is that the surface tension varies with the charge in the same way as the potential varies with the surface area [15,16]

$$\frac{\partial\gamma}{\partial q} = \frac{\partial\varphi}{\partial\theta}, \qquad (3)$$

(the derivative $\partial\varphi/\partial\theta$ is obtained for a constant overall electrode charge). Hence follows also the equation

$$\frac{\partial\gamma}{\partial\varphi} = -q - \frac{\partial q}{\partial\theta}. \qquad (4)$$

After Eqn. (3) had been suggested by experiment, it became clear that it should follow from thermodynamics. However, until the elastic charging effect had been observed there was no reason to compare the two derivatives. Furthermore, in the thermodynamics of surface phenomena it is simpler to formulate the equation than to elucidate the significance of the quantities involved in it. An example is provided by Young's simple equation for the angle of wetting of a solid by a liquid, which was proposed in 1805.[17] However, controversy concerning the physical significance of its variables is still continuing, namely whether these are forces acting along three interfaces or whether they represent the work of formation of these interfaces [18,19].

In the absence of experiments on elastic charging the significance of the quantity θ in Eqn. (3) would have remained obscure, i.e. it would not have been known whether it represents elastic or plastic deformation. On the other hand, if one could imagine an effect opposite to that of the potential on the wetting angle, the significance of the quantities in Young's equation would become clearer.

3. The Equation for the Wetting of Solid Electrodes

Frumkin and coworkers [20-22] have made systematic studies on the influence of the potential on the wetting of liquid electrodes. At the boundary between the electrode and a gas bubble a conducting electrolyte film was observed [21]. The publication of studies specially devoted to the wetting of solid electrodes began recently. A series of detailed studies by Morcos, in which measurements were made of the wetting angle for a planar solid electrode as a function of potential [23-26], and the investigation of Bonnemay et al. [27] are noteworthy.

Below we shall describe an approach to the problem based on the relation between the forward and reverse effects. Consider a solid electrode of arbitrary shape partly immersed in a liquid electrolyte solution (for example a half-immersed rectangular plate). Suppose that z is the vertical coordinate of the electrode (the depth of immersion is reckoned from the horizontal level of the liquid solution), $\mathcal{P}$ the weight of the partly immersed electrode for a fixed z (the force experienced by the object from which the electrode is suspended), Q the overall charge of the electrode, and φ the potential of the electrode relative to a reference electrode immersed in the same electrolyte. If the remaining parameters of the system are kept constant, the total differential of its free energy is

$$dF = -\mathcal{P}dz + \varphi dQ \quad . \qquad (5)$$

Hence we obtain the fundamental equations

$$\frac{\partial\mathcal{P}}{\partial Q} = -\frac{\partial\varphi}{\partial z}, \qquad (6)$$

$$\frac{\partial\mathcal{P}}{\partial\varphi} = \frac{\partial Q}{\partial z} \qquad (7)$$

representing the change in the weight of the partly immersed electrode when the change in potential corresponds to the change in the charge of the electrode on immersion.

Suppose further that the electrode has a cylindrical surface with a vertical generatrix and directrix of arbitrary form (for example, a vertical plate). The contour of the horizontal section through the electrode at the level of the solution at a point remote from the meniscus will be called the water line of the electrode. The wetting boundary does not coincide with this line and is not in the general case a two-dimensional curve. For example, at

the edges of the plate the meniscus is below its position in the central part of the plate. We introduce the following notation: s is the length of the water line and, what amounts to the same thing, the perimeter of the electrode cross-section and q_i and q_n are the charge densities on the immersed and unimmersed parts of the electrode respectively. If the electrode is not smooth, then q_i and q_n must be replaced in the corresponding formulae by αq_i and αq_n, where α is the roughness factor. The overall charge of the electrode is $Q = s[zq_i + (H - z)q_n]$, where H is the height of the electrode. Since the densities q_i and q_n are independent of z, it follows that $(\partial Q/\partial z)/s = q_i - q_n$. On substituting this in Eqn.(7), we obtain the equation for the wetting of solid electrodes:

$$\frac{1}{s}\frac{\partial \mathcal{P}}{\partial \varphi} = q_i - q_n. \qquad (8)$$

This is the fundamental equation. It makes it possible to determine $q_i - q_n$ directly from the dependence of the weight of the electrode on the potential. No restrictions are then imposed on the form of the electrode cross-section and the shape of the meniscus. The non-uniformity of the wetting line is permissible, for example the fall of the meniscus at the edges of the plate.

The following formula was obtained similarly:

$$\frac{1}{s}\frac{\partial \mathcal{P}}{\partial \mu} = \Gamma_i - \Gamma_n, \qquad (9)$$

where μ is the chemical potential of the adsorbable substance and Γ_i and Γ_n are the relative surface amounts of this substance on the immersed and unimmersed parts of the electrode respectively (relative to the simultaneous adsorption of the solvent).

Under conditions where q_n is independent of φ, the differential equation (8) yields

$$\frac{1}{s}\frac{\partial^2 \mathcal{P}}{\partial \varphi^2} = C, \qquad (10)$$

where $C = \partial q_i/\partial \varphi$ is the differential capacitance of the electrode. The minimum weight $\mathcal{P}$ is reached when $q_i = q_n$.

A force equal to the weight of the meniscus is applied to the electrode along the wetting line. We project a small section of this line on to the water line. The ratio of the corresponding fraction of the weight of the meniscus to the length of the projection will be called the weight tension $\mathscr{C}$. The weight tension is the same at all points on the water line for any shape of the latter. Thus the weight of the meniscus is $s\mathscr{C}$. For this reason Eqn.(8) can be rewritten as follows:

$$\frac{\partial \mathscr{C}}{\partial \varphi} = q_i - q_n. \qquad (11)$$

Formulae referring to special types of electrodes follow from Eqn.(8). Suppose, for example, that the electrode consists of a thin layer of metal deposited on the inner surface of a capillary with radius a and that the capillary contains a column of electrolyte with a height h and density ρ. Then $s = 2\pi a$ and $\mathcal{P} = \pi a^2 h\rho$ (the weight of the liquid in the capillary) to within constant terms. Eqn.(10) immediately yields the following result:

$$\frac{\rho a}{2}\frac{\partial^2 h}{\partial \varphi^2} = C, \qquad (12)$$

which agrees with the formula obtained previously by Bonnemay by differentiating Young's equation and by examining the geometry of the meniscus in the capillary [27]. Measurement of the height of the rise of the liquid by an optical method (involving the passage of X-rays through the liquid [27]) is associated with errors comparable to the radius of the capillary.

However, it follows from the general equation (8) that there is no need to consider the geometry of the meniscus, to make separate calculations for each shape of the electrode, and to measure a specific parameter characteristic of each given electrode. It is sufficient to measure the influence of the potential on a parameter common to all electrodes, namely their weight. This greatly simplifies the experiment, increasing its accuracy and sensitivity.

The weight tension $\mathscr{C}$ is related to the wetting angle θ and the surface tension of the liquid by the expression

$$\mathscr{C} = \sigma_0 \cos\theta. \qquad (13)$$

Hence we obtain from Eqn.(11)

$$q_i - q_n = -\sigma_0 \sin\theta \frac{\partial \theta}{\partial \varphi}. \qquad (14)$$

Eqns.(8) and (11) are applicable to isotropic and anisotropic surfaces. The charge densities on the right-hand side of Eqn.(11) are independent of the orientation of the anisotropic surface following immersion. Consequently $\mathscr{C}$ is a scalar quantity. It characterises the work of wetting and has no bearing on the surface tension of the solid, which is a tensor. The quantities entering into Young's equation are also scalar and cannot be identified with forces. On the other hand, owing to the term $\partial q/\partial \theta$, which depends on the direction of deformation, Eqn.(4) defines a tensor—the surface tension γ.

4. The Surface Tension and the Work of Formation of the Surface of a Solid Electrode

The difference between the surface tension of a solid γ and the reversible work of formation of its unit surface σ, noted 100 years ago by Gibbs [28], has not so far been confirmed experimentally owing to the lack of data for the surface tensions of solids. The results of the present study permit such a comparison at the level of derivatives of these quantities with respect to the potential.

Fig. 9 illustrates the variation of $\partial\gamma/\partial\varphi$ and $\partial\sigma/\partial\varphi$ with potential φ for platinum in 1 N H_2SO_4; $\partial\gamma/\partial\varphi$ was measured by the estance method and $\partial\sigma/\partial\varphi$ is equal, according to Lippman's equation, to the total charge density q of the platinum electrode, the dependence of which on the potential was measured for the first time by Frumkin and coworkers [3]. The difference between the two quantities is large: like the charge, $\partial\sigma/\partial\varphi$ varies monotonically with potential, while $\partial\gamma/\partial\varphi$ passes through zero three times in the hydrogen potential range. Accordingly the integrated relation between the surface tension of the platinum electrode and the potential has three extrema—two maxima at +0.1 and +0.2 V (relative to the potential of the reversible hydrogen electrode) with an intervening minimum.

After substracting q from the φ-estance in accordance with Eqn.(4), we obtain $\partial q/\partial\theta$—the change in charge density as a result of elastic deformation at a constant potential. The variation of $\partial q/\partial\theta$ with φ is indicated by a dashed line; hence it is clear that, in the system under consideration, the term $\partial q/\partial\theta$ in Eqn.(4) predominates over the term q and largely determines the variation of γ with φ.

Thus the experimental data obtained by the estance method demonstrate a difference between the surface tension of a solid and the reversible work of formation of its

unit surface and also that this difference obtains in the region of electrocapillary phenomena. The latter had been overlooked until the present investigation.

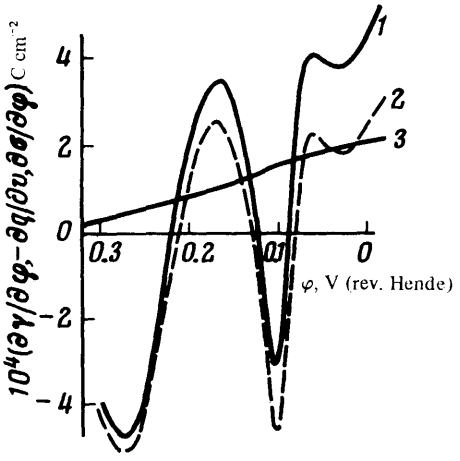

Figure 9. The difference between the surface tension γ and the work of formation of unit surface area σ of a solid electrode at the level of derivatives of these quantities with respect to the potential φ for platinum in 1 N H_2SO_4: 1) $\partial\gamma/\partial\varphi$; 2) $-\partial q/\partial\theta$; 3) $\partial\sigma/\partial\varphi$.

5. The Surface Tension of a Rough Surface

Suppose that the rough interface coincides with one of the sides of the plate and that α is the roughness factor: the ratio of the area of the rough surface Ω to the area of its average plane Ω_0 is $\alpha = \Omega/\Omega_0$. The surface tension γ directed along rugosities deforms the plate as a whole in a specific manner. It is necessary to find γ_0, acting uniformly, which when directed along the plane would give rise to the same deformation. For each specific electrode, the results of the surface tension and elastic charging methods should coincide regardless of whether the electrode surface is smooth or rough. Hence, and also on the basis of the principle of the reciprocity of the displacements, it was found that the increments in the tensions γ_0 and γ refer to the increments of the areas Ω and Ω_0 on elastic deformation. We call the ratio

$$\beta = \Delta\Omega/\Delta\Omega_0 = \Delta\gamma_0/\Delta\gamma \qquad (15)$$

the differential roughness factor. In many cases the model of a rough surface with rugosities in the form of parallel ridges with a symmetrical triangular cross-section is applicable. For an isotropic surface, consisting of sections with ridges running in random directions[13], we have

$$\beta = \frac{1}{2}[(1-\nu)\alpha + (1+\nu)\alpha^{-1}]. \qquad (16)$$

For example, for lead ($\nu = 0.44$) the deviation of β from unity on such a surface does not exceed 11% in the range $1 \leq \alpha \leq 3$.

The knowledge of β permits the determination of the true estance from its planar equivalent (subscript 0) measured experimentally. For φ- and q-estance, we have

$$\frac{\partial\gamma_0}{\partial\varphi} = \beta\frac{\partial\gamma}{\partial\varphi}; \quad \frac{\partial\gamma_0}{\partial q_0} = \frac{\beta}{\alpha}\frac{\partial\gamma}{\partial q}. \qquad (17)$$

6. Discrepancies Between the Forward and Reverse Effects

Among the irreversible processes which disturb the correspondence between the results of surface tension and elastic charging measurements, the Faraday diffusion current, caused by the presence of traces of electrochemically active substances in solution, is encountered most frequently. Stirring is known to increase this current. A strip undergoing longitudinal deformation stirs the solution much less than a transversely vibrating suprameniscus electrode. This in fact dictated the choice of a strip for recording elastic charging.

It is interesting that the diffusion current does not influence at all the result of measurements of oscillating surface tension (it is smaller by several orders of magnitude than the specified charging current amplitude). This is the reason for the discrepancies and demonstrates at the same time the advantages of the surface tension method. Hence it is also seen that the agreement between the surface tension and elastic charging data is not predetermined beforehand and that even the discrepancies between these data can lead to useful conclusions about the test object.

Noting the similarity between the data derived by the two methods, we began with the first harmonics of the quantities recorded by them—the surface tension and the potential. At the level of the highest harmonics the two methods yield different information even in reversible systems.

IV. SOME PROBLEMS OF THE THEORY OF ESTANCE

1. The Surface Tension Increment

Consider a solid electrode in a solution containing, together with a solvent, m components which are electrically neutral overall. The electrode potential φ is specified relative to a reference electrode, which is reversible with respect to one of the ions forming part of the electrolyte. In the general case the change in the surface tension of the solid electrode γ is described by the equation[15]:

$$d\gamma = -\left[q + \left(\frac{\partial q}{\partial\theta}\right)_{\varphi,\mu_k}\right]d\varphi - \sum_{s=1}^{m}\left[\Gamma_s + \left(\frac{\partial\Gamma_s}{\partial\theta}\right)_{\varphi,\mu_k}\right]d\mu_s, \qquad (18)$$

where q is the electrode charge density, Γ_s and μ_s are the excess amounts on the surface relative to the solvent and the chemical potentials of the solution components, θ is the relative change in the area of the electrode during its elastic deformation, and $k, s = 1, \ldots, m$.

2. Indication of Localised Adsorption

The slope of the estance–potential curve is characterised by the derivative $\gamma_{q\varphi} = \partial(\partial\gamma/\partial q)/\partial\varphi$. The amplitude of the second harmonic of the potential at a specified

sinusoidal current is proportional to the derivative $\varphi_{qq} = \partial^2\varphi/\partial q^2$. On metallic electrodes in the absence of localised adsorption, $\gamma_{q\varphi} = -1$ both at the zero-charge point and at the zero points of the second harmonic:

$$\gamma_{q\varphi} = -1 \text{ when } q = 0 \text{ or } \varphi_{qq} = 0. \quad (19)$$

Under the same conditions, $\gamma_{q\varphi}$ at zero estance is

$$\gamma_{q\varphi} = -1 + \frac{\partial\varphi_0}{\partial\vartheta}\frac{1}{C}\frac{\partial C}{\partial\varphi} \text{ when } \gamma_q = 0, \quad (20)$$

where C is the differential capacitance of the electrode and

$$\frac{\partial\varphi_0}{\partial\vartheta} = \frac{\partial\gamma}{\partial q}\Big|_{\varphi=\varphi_0} \quad (21)$$

is the shift of the zero-charge potential φ_0 on elastic deformation of the electrode. For non-localised adsorption, this quantity does not exceed 0.03 V [29] and the property $\gamma_{q\varphi} = -1$ therefore persists to within at least 10% also at zero estance.

The deviation of the slope $\gamma_{q\varphi}$ from unity at the above points is a sufficient indication of localised adsorption. For cadmium in 0.01 M NaF, the slope of the estance–potential curve at zero estance (and at the point where $q = 0$) is close to -3. Hence we conclude that water is locally adsorbed on cadmium [29].

3. The Estance of the Diffuse Double Layer

If the fluidity of the liquid electrolyte persists up to its boundary with the dense part of the double layer, elastic deformation does not alter the parameters of the diffuse layer. Under these conditions, at the zero-charge point and a low electrolyte concentration a, the following relation holds:

$$\gamma_{q\varphi} = -1 - B\sqrt{a} \text{ when } \varphi = \varphi_0, \quad (22)$$

where B is a constant independent of a. On dilution and therefore on increase of the thickness of the diffuse part of the double layer, the slope $\gamma_{q\varphi}$ tends to unity regardless of the structure of the dense part of the double layer.

The fluidity condition probably does not hold in all systems. On dilution, an appreciable decrease of the slope should occur for cadmium in aqueous NaF solutions. However, up to a concentration of 0.001 M, this effect is not observed, which suggests that on cadmium there is a locally adsorbed polymolecular film of water in which the diffuse part of the double layer adjoining the electrode is accommodated; this film has an ordered structure but retains the defects characteristic of the liquid in the form of migrating vacancies, which permits the motion of ions at the electrode and preserves nearly normal capacitance values.

4. The Estance of a Solid *in Vacuo*

Consider a planar condenser consisting of identical plates *in vacuo*, whose electron work function is φ_{0V}. When an alternating current is passed through the condenser and the average stress applied to its plates is zero (for example the plates are connected to the secondary winding of a transformer), the oscillations of the surface tension γ of each plate at the current frequency can be measured. Then [30]

$$\frac{\partial\gamma}{\partial q} = \frac{\partial\varphi_{0v}}{\partial\vartheta}, \quad (23)$$

i.e. the estance is equal to the change in the electron work function on elastic deformation of the specimen.

5. The Introduction of Elastic Deformation into the Adsorption Isotherm

When electrically neutral species are adsorbed from the solution, their chemical potential in solution μ is independent of the electrode potential φ. At a constant value of φ the surface concentration of these species Γ is a function of μ and of the relative change in the area of the electrode on elastic deformation θ: $\Gamma = \Gamma(\mu, \theta)$. In its usual sense [4], the adsorption isotherm defines the variation of Γ with μ in the absence of deformation (when $\theta = 0$):

$$\Gamma = \Gamma(\mu, 0) = f(\mu). \quad (24)$$

Suppose that

$$\xi(\mu, \vartheta) = \frac{\partial\gamma}{\partial\Gamma}(\mu, \vartheta) \quad (25)$$

is the contribution of the adsorbed species to the surface tension known on the basis of experimental data to be a function of both μ and θ. Then expansion of Γ in powers of θ is

$$\Gamma(\mu, \vartheta) = f - \vartheta(f + f'\xi) + \frac{1}{2}\vartheta^2[f + f'(2\xi + \xi\xi_\mu - \xi_\vartheta) + f''\xi^2], \quad (26)$$

where

$$f' = df/d\mu,\ f'' = d^2f/d\mu^2,\ \xi_\mu = \partial\xi/\partial\mu,\ \xi_\vartheta = \partial\xi/\partial\vartheta.$$

6. The Increase of Estance with the Thickness of the Polarised Layer

In many systems, for example on platinum and tungsten, in aqueous solutions at fairly anodic potentials the estance increases with the degree of oxidation of the surface (the capacitance curves corresponding to different degrees of oxidation are superimposed in Fig. 5*b* on the estance curves; a decrease of the capacitance curve is accompanied by a rise of the estance curve). The increase of estance with the thickness of the coating, in the given instance an oxide coating, is a sign of the existence of an intrinsic dipole moment of the coating and is described by the expression [31]

$$\frac{\partial\gamma}{\partial q} = \left(-1 + \frac{\partial\delta}{\partial\vartheta} - \frac{\partial w}{\partial\vartheta}\right)(\varphi - \varphi_n) + \left(\frac{\partial\delta_0}{\partial\vartheta} - \frac{\partial\delta}{\partial\vartheta}\right)\frac{P}{\varepsilon}\mathfrak{h} + \frac{\partial\varphi_n}{\partial\vartheta}, \quad (27)$$

where P is the intrinsic polarisation of the coating (the dipole moment per unit volume), ϵ the effective dielectric constant of the coating, θ the relative change in the area of the electrode on elastic deformation, w, δ, and δ_0 are the relative values of the dielectric constant, the thickness of the coating, and the length of one arm of the dipole respectively, φ_n is the zero-charge potential of the oxidised electrode extrapolated to zero thickness of the oxide film, and $\mathfrak{h}$ the effective thickness of the coating, whose significance is retained at coverages less than the monolayer value, equal to the ratio of the volume occupied by the coating to the area of the electrode.

V. THE INFLUENCE OF BULK-PHASE FORCES ON THE ELECTRODE

1. Inertial Oscillation of the Electrolyte on Passage of an Alternating Current

Suppose that an electrolyte solution is in a long open channel and that a current at a density $j = \Delta j \sin\omega t$, where t is the time and $\omega/2\pi$ the frequency, passes along the

channel. Then at points remote from the walls of the channel the solvent coordination system is displaced relative to the laboratory coordinate system at the rate [7,32]

$$v_0 = (\Delta j/F\rho)\,\mathbf{M}\sin\omega t, \tag{28}$$

where F is the Faraday, ρ the density of the solution,

$$\mathbf{M} = \tau_a(m_a - \rho_0\psi_a) - \tau_c(m_c - \rho_0\psi_c) \tag{29}$$

the reduced mass, τ, m, and Ψ are respectively the transport number, the gram-ionic weight, and the apparent ionic volume of the anion (subscript a) and the cation (subscript c), ρ_0 is the solvent density, and Ψ_a and Ψ_c are the fractions of anions and cations in the volume displaced from the pure solvent on dissolution of one equivalent of the electrolyte; these values have been determined recently by several methods and are quoted in the literature [33,34].

2. The Viscous Force of the Electrolyte

The wall of the channel through which the sinusoidal current is flowing within the electrolyte is acted upon by a viscous force [32]

$$g = \sqrt{\omega\chi}\,(\mathbf{M}\Delta j/F)\cos\left(\omega t + \frac{3}{4}\pi\right), \tag{30}$$

where χ is the kinematic viscosity of the solution; the force g is referred to unit area of the wall. It is manifested independently of the electrophoretic force.

Under the conditions of estance measurements, the alternating current flows only at right angles to the surface of the electrode, which does not therefore experience a tangential force. However, it is possible to devise a special experiment where conditions are created such that the alternating current in the electrolyte flows only parallel to the electrode surface. Then the surface is acted upon by the force g.

3. Generation of Ultrasound at the Electrode

Suppose that the electrode is absolutely rigid and consists of a plane bounding half the space of the electrolyte (this condition holds, for example, for a metallic membrane both sides of which are active to an equal extent). Then the pressure on the electrode caused by the displacement of the centre of gravity [7] in the volume of electrolyte adjoining the electrode on passage of the alternating current is $p_0 = -\Delta p_0 \sin\omega t$ with the amplitude

$$\Delta p_0 = u\mathbf{M}\Delta j/F, \tag{31}$$

where u is the velocity of sound in the solution.

The electrode processes also contribute to the pressure. For example, the passage of one equivalent of cations from the bulk of the electrolyte to the surface of the electrode leads to an increase of the overall volume of the layer near the electrode by $V_{ce} - V_{cs}$, where V_{ce} and V_{cs} are the partial equivalent volumes of the cation in the double layer and in the electrolyte respectively. The heat evolved at the electrode on passage of one equivalent of electricity, which increases the volume near the electrode by a certain amount (by $V_\Pi = \Pi F\beta/\zeta\rho$ for a thin membrane, where β is the coefficient of cubic expansion of the solution, ζ the specific heat of the solution, and Π the effective Peltier coefficient). Thus the overall pressure amplitude in the given case is

$$\Delta p = u(\Delta j/F)\,[\mathbf{M} + \rho(V_{ce} - V_{cs} + V_\Pi)]. \tag{32}$$

On electrodeposition, V_{ce} is replaced by the equivalent volume of the metal. The quantity ρV_Π is of the order of 0.1 g equiv.$^{-1}$ for non-polarisable electrodes and is virtually zero for polarisable electrodes.

4. Diffusion Waves at the Electrode

Suppose that an electrically neutral substance present in the bulk of the electrolyte and supplied to the electrode via diffusion undergoes periodic adsorption and desorption at the electrode–electrolyte interface. If m is the molecular weight of the test substance, V_{ns} its partial molar volume in the solution, D its diffusion coefficient, and $c(x,t)$ its concentration at a distance x from the electrode at time t, then mass transport as a result of the diffusion of the substance in the layer near the electrode leads to a variable pressure:

$$p_v = D(m - \rho V_{ns})\,\partial c/\partial t\,(0,t)\ . \tag{33}$$

It is remarkable that the pressure p is completely independent of the distribution of the substance in the electrolyte and is determined solely by the rate of change of its concentration at the surface of the electrode.

Another component of the pressure, due to the change in the volume of the layer near the electrode caused by adsorption, is taken into account in the same way as in the electroadsorption of cations discussed above.

5. The Mass Attached to the Electrode

For an electrode with identical current densities on both sides (a vertically immersed plate, a foil strip), the pressures experienced by these two sides fully cancel out and have no influence on the results of estance measurements. The pressure applied to a narrow supramениscus electrode, only one side of which is operative, differs from that which was defined above relative to an absolutely rigid electrode infinite in extent.

Like the deformation of a solid electrode occurring when the surface tension changes, the linear velocity of the electrode vibrations is so small that viscous forces may be neglected and the electrode may be assumed to move in a non-viscous liquid. Since the supramениscus electrode can be in contact with its electrolyte, the electrolyte oscillating at a frequency v_0 acts on the electrode with a force $G_0 = -m_0(dv_0/dt)$, where m_0 is the mass attached to the electrode. On the other hand, the inertial force due to the transverse vibrations of the electrode itself when the surface tension is altered amounts to $G_e = -m_e(dv_e/dt)$, where v_e is the velocity of the electrode and m_e its mass. The acceleration dv_0/dt is smaller by two orders of magnitude than dv_e/dt. Furthermore, usually $m_0 \ll m_e$. As a result of this, the pressure hardly distorts the estance measurements with the aid of the supramениscus electrode. Electrodes of special shape, for which the influence of the transverse surface tension is compensated, are used to record the pressure.

6. Diffusion of the Electrolyte and Thermal Vibrations of the Electrode

Heating of the electrolyte by the sinusoidal current leads to thermal vibrations of the electrode at twice the current frequency. The electrode is acted upon at the same frequency by the second harmonic of the surface

tension [35]. For each of these two effects, there is a special form of the alternating current (other than sinusoidal) for which the influence of the second effect is fully ruled out. In particular, thermal vibrations of the electrode can be distinguished.

Only a thin layer of electrolyte is involved in the transfer of heat from the electrolyte to the electrode. Its thickness $b = \sqrt{2D_T/\omega}$ decreases at a frequency $\omega/2\pi$; D_T is the thermal diffusivity of the liquid electrolyte. Suppose that the electrolyte consists of two components at concentrations c_1 and c_2 (in equivalents) and with the equivalent conductances Λ_1 and Λ_2, which are independent of concentration in dilute solutions. The steady-state values of c_1 and c_2, which are equal to those in the bulk of the solution, are designated by c_{10} and c_{20}. We introduce the parameter $v = c_{20}c_2/c_{10}c_1$. When the concentration near the electrode c_1 changes abruptly from c_{10} to 0, the thickness of the diffusion layer is defined by the expression $d = \sqrt{\pi D_C t}$, where t is the time elapsed from the instant of the concentration jump and D_C the effective diffusion coefficient taking into account the migration in the electric field. We introduce the notation

$$\lambda = \frac{d}{b} = \sqrt{\frac{\pi}{2}\frac{D_c}{D_\tau}\omega t}; \qquad (34)$$

$\mathfrak{P}$ is the ratio of the amplitudes of the thermal vibrations of the electrode before and after the concentration jump for the same alternating heating current.

Suppose that $\lambda \gg 1$ and $\lambda v \ll 1$; the thickness of the diffusion layer is then large compared with that of the thermal layer, but the c_1 concentration drop in the thermal layer continues to be greater than the background concentration c_{20}. Then

$$\mathfrak{P} = \sqrt{2}\lambda(1+v)e^{\lambda v}\sqrt{[\mathfrak{C} + \ln(\sqrt{2}\lambda v) - \lambda v]^2 + \left(\frac{\pi}{4} - \lambda v\right)^2}, \qquad (35)$$

where $\mathfrak{C} = 0.5772$ is the Euler constant.

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Electrochemical Processes in an Alternating Current

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The theory of electrochemical impedance is reviewed. Alternating current circuits equivalent to an electrochemical reaction proceeding via an adsorption state are examined for reversible and irreversible systems. The dynamic adsorption equation for a non-equilibrium electrode is discussed. The theoretical circuits are compared with experimental data for the iodine-iodide system.
The bibliography includes 59 references.

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I. INTRODUCTION

The use of alternating current in electrochemistry has a long history. The first studies of these lines were begun as early as the 19th century and were associated with the measurement of the conductivities of electrolytes[1]. However, at that time it was already noted that the overall resistance of the electrochemical cell to the alternating current includes the resistance of the electrode–electrolyte boundary. Warburg[2] and Kruger[3] obtained equations for electrode impedance in the special case of diffusion-controlled electrode processes and attempted to measure it. However, the lack of a sufficiently deep understanding of the mechanism of electrochemical reactions and of a reliable experimental technique resulted in comparatively little development in this field — the alternating current was used for a long time exclusively for conductimetric studies.

A decisive breakthrough occurred only after studies by Frumkin and coworkers[4,5], in which the capacitance of the electrical double layer of an ideally polarised mercury electrode was determined for the first time by direct measurements in an alternating current and a capacitance minimum was observed in dilute aqueous solutions at the zero-charge potential, which constituted experimental confirmation of the diffuse double layer theory. Somewhat later Dolin, Ershler, and Frumkin[6–8] used alternating current to investigate the kinetics of the evolution of hydrogen on a platinum electrode. These studies began the wide-scale employment of alternating current in electrochemical kinetics[9–21]. Quantitative measurements of the impedance of readily polarisable electrodes have recently undergone a fresh development and have been discussed in detail in a number of reviews[22–27].

II. IMPEDANCE OF SLOW ELECTROCHEMICAL REACTIONS

The main property of cells with ideally polarisable electrodes is that their impedance corresponds to the simplest a.c. circuit comprising the series-connected electrolyte resistance R_e and the double-layer capacitance C_d (Fig. 1*a*):

$$Z = R_e + (j\omega C_d)^{-1}. \quad (1)$$

The rate of relaxation of the double layer in solutions is fairly high, so that, even at frequencies of the order of several Megahert, C_d (as well as R_e) is independent of the a.c. frequency[28,29]. For comparatively slow electrode processes, it is possible to isolate three classical mechanisms under these conditions.

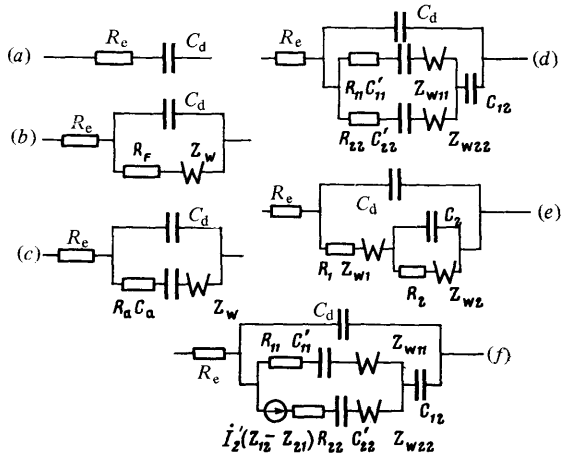

Figure 1. Equivalent a.c. circuits.

1. An electrochemical reaction not accompanied by the adsorption of the reactants: the Ershler–Randles impedance[30–32]. The process is illustrated graphically in Fig. 2*a* and the equivalent a.c. circuit is shown in Fig. 1*b*. The corresponding analytical expression for the impedance is

$$Z = R_e + \{j\omega C_d + [R_F + \tilde{W}/\sqrt{j\omega}]^{-1}\}^{-1}, \quad (2)$$

where

$$R_F = RT/(nF)^2 V_0 \quad (3)$$

is the resistance to charge transfer,

$$\tilde{W} = RT/(nF)^2 c_0 \sqrt{D} \quad (4)$$

the Warburg constant, i_0 the exchange flux for the charge-transfer reaction, c_0 the concentration of electrochemically active species in the bulk of the electrolyte, D their diffusion coefficient, F the Faraday, and n the number of charges transported in an electrochemical reaction of the type

$$Ox + ne \rightleftharpoons Red. \tag{5}$$

The expression in square brackets in Eqn. (2) is called the Faraday impedance (Z_F).

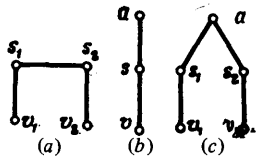

Figure 2. Schematic graphical representation of electrode processes.

2. An adsorption process without electrochemical reaction: the Frumkin–Melik–Gaikazyan impedance[33,34]. The process is illustrated by a graphical scheme in Fig. 2 and the equivalent a.c. circuit is shown in Fig. 1*c*:

$$Z = R_\Omega + \{j\omega C_d + [R_a + \tilde{W}_a/\sqrt{j\omega} + (j\omega C_a)^{-1}]^{-1}\}^{-1}, \tag{6}$$

where

$$\left.\begin{aligned} R_a &= RT/q_A^2 V_0;\ C_a = q_A^2/\tilde{\mu}_A, \\ \tilde{W}_a &= RT/q_A^2 c_0 \sqrt{D}, \end{aligned}\right\} \tag{7}$$

q is the electrode charge, A the amount of substance in the adsorbed state, $\tilde{\mu}$ the electrochemical potential of the adsorbed substance, $q_A = (\partial q/\partial A)\varphi$, and $\tilde{\mu}_A = (\partial\tilde{\mu}/\partial A)\varphi$. Here both C_d and C_a make up the double layer capacitance; although the charging of the C_d capacitance is rapid, the C_a capacitance charges slowly and the kinetics of its charging process are determined by the rates of adsorption (R_a) and diffusion ($\tilde{W}_a$) of the species undergoing adsorption, for example dipolar organic molecules.

3. An electrochemical reaction complicated by a chemical reaction: the Gerischer impedance[35–37]. In contrast to the Ershler–Randels impedance, in this case the electrochemically active species appear near the electrode both as a result of diffusion and as a result of a chemical reaction, for example the decomposition of a complex. For this reason the Warburg impedance in the usual circuit (Fig. 1*b*) is replaced by a complex resistance, which depends on the frequency in a more complicated manner (see, for example, Vetter[13]).

III. IMPEDANCE OF ELECTROCHEMICAL REACTIONS COMPLICATED BY ADSORPTION

The theory of the impedance of electrochemical reactions complicated by adsorption has been developed since 1961.[21,38–47] Fig. 2*c* illustrates a schematic graphical representation of a reaction proceeding via an adsorbed state. A characteristic feature of such processes is that charge transfer from the reacting species to the metal can in general take place in two stages. In the first stage (line s_1a) the oxidised form passes from the state near the surface of the electrode (point s_1) to the adsorbed state (point a). This entails the transfer of a charge n_1. In the second stage (line as_2) the substance passes from the adsorbed state in the reduced form to the state near the electrode surface (point s_2). This entails the transfer of a charge n_2. The overall number of electrons supplied to the electrode via the external circuit on transition of the reactant from point s_1 to point s_2 is n under the conditions of a constant potential, so that

$$n_1 + n_2 = n; \tag{8}$$

here n_1 and n_2 need not be integral numbers. Only their sum n is an integar. The quantities n_1 and n_2 are macroscopic characteristics— they define the amount of electricity which is supplied on average to the electrode via the external circuit when an ion or molecule of the surface-active substance passed from one state to another.

Following Lorenz and Salie[39], we put

$$n_1 = ln;\ n_2 = (1-l)n\ . \tag{9}$$

The coefficients l and $1-l$ characterise the fraction of the charge transferred in each of the two adsorption stages. The charge transfer in the individual stages of the electrochemical reaction can be related to the adsorption characteristics of the system[21,48]:

$$l = \frac{\Gamma_{1\mu_1} + \Gamma_{1\mu_2}}{\Gamma_{1\mu_1} + \Gamma_{2\mu_2} + \Gamma_{1\mu_2} + \Gamma_{2\mu_1}}, \tag{10}$$

where Γ_1 and Γ_2 are respectively the Gibbs adsorptions of the oxidised and reduced forms μ_1 and μ_2 are their chemical potentials, and $\Gamma_{1\mu_2} = \Gamma_{2\mu_1}$. This relation makes it possible to calculate the charge transferred from thermodynamic data for the overall charges of the reversible electrode. Such calculations have been made, for example, for charge transfer in the adsorption of H^+ ions and hydrogen atoms on a platinum electrode[48]. It was found that in this system the parameter l varies markedly with the potential and also depends on the composition and pH of the solution. In many cases l is greater than unity. In other words, in the adsorption of H^+ ions, excess negative charge can be transferred to them.

The impedance of an electrochemical reaction proceeding via two adsorption stages can be calculated using the method of equivalent multiterminal networks and Onsager's reciprocal relations[21,43,44]. Although from the standpoint of the theory of electric circuits the electrochemical cell always consists of a two-terminal network (diode), in the presence of a two-stage process an individual current corresponds to each stage (I_1 and I_2). However, since adsorption processes do not tkae place independently because we are dealing with reactions of the same substance, the currents I_1 and I_2 are related. This can be expressed with the aid of relations between the current and polarisation analogous to the equations for a four-terminal network:

$$\left.\begin{aligned} \Delta\varphi &= Z_{11}I_1 + Z_{12}I_2, \\ \Delta\varphi &= Z_{21}I_1 + Z_{22}I_2, \end{aligned}\right\} \tag{11}$$

where Z_{11} and Z_{22} are the input impedances for two adsorption processes (s_1a and s_2a) and Z_{12} and Z_{21} describe the interaction of these processes.

Eqns. (11) characterise a four-terminal network, which is the electrical equivalent of the given process. A characteristic feature of such a four-terminal network is that the potentials at the two pairs of its terminals are the same

and equal to $\Delta\varphi$. Eqns. (11) express in essence the phenomenological law of non-equilibrium thermodynamics as applied to electrochemical reactions. Since in the absence of an alternating current the system is at equilibrium, the Onsager relation $Z_{12} = Z_{21}$ (the equality of the kinetic cross-coefficients) should hold. Direct calculations for this process, illustrated schematically in Fig. 2*c*, show that the frequency dependences of the coefficients Z_{12} and Z_{21} are in fact the same and their equality can be confirmed independently by analysing the Gibbs adsorption equation (or more precisely the equality of the cross-derivatives of the Gibbs adsorptions of the two forms with respect to the chemical potentials $\Gamma_1\mu_2 = \Gamma_2\mu_1$).[21,46]

The Faraday impedance, calculated by Eqns. (11), can be formulated as follows:

$$Z_F = \frac{Z_{11}Z_{22} - Z_{12}^2}{Z_{11} + Z_{22} - 2Z_{12}}, \qquad (12)$$

where

$$Z_{11} = R_{11} + \widetilde{W}_{11}/\sqrt{j\omega} + (j\omega C_{11})^{-1}, \qquad (13)$$

$$Z_{22} = R_{22} + \widetilde{W}_{22}/\sqrt{j\omega} + (j\omega C_{22})^{-1}, \qquad (14)$$

$$Z_{12} = -(j\omega C_{12})^{-1}, \qquad (15)$$

and the coefficients R_{11}, C_{11}, $\widetilde{W}_{11}$, etc. are expressed in terms of parameters characterising the electrochemical reaction:

$$R_{ii} = RT/(n_iF)^2V_{i0};\ \widetilde{W}_{ii} = RT/(n_iF)^2c_{i0}\sqrt{D_i};\ C_{ik} = n_in_kF^2/\widetilde{\mu}_A, \qquad (16)$$

where $i, k = 1$ or 2. The equivalent a.c. circuit for the given process can be constructed, for example, in the way shown in Fig. 1*d*. In this case we have

$$(C_{ii}')^{-1} = C_{ii}^{-1} + C_{ik}^{-1}\ (i \neq k). \qquad (17)$$

In order to represent the Faraday impedance in a fairly compact analytical form, we introduce the following notation:

$$l/(1-l) = \xi, \qquad (18)$$

$$c_{10}\sqrt{D_1}/c_{20}\sqrt{D_2} = r;\ V_{10}/V_{20} = p\ . \qquad (19)$$

Then Eqn. (12) can be reduced to the form

$$Z_F = \frac{\widetilde{W}_{11}C_{11}^{-1}(1+r)\xi^2x^3 + [R_{11}C_{11}^{-1}(1+p) + \widetilde{W}_{11}^2r]\xi^2x^2 + R_{11}\widetilde{W}_{11}(p+r)\xi^2x + pR_{11}\xi^2}{C_{11}^{-1}(1+\xi)^2x^2 + \widetilde{W}_{11}(1+r\xi^2)x + R_{11}(1+p\xi^2)}, \qquad (20)$$

where $x = (j\omega)^{-1/2}$.

The case where the effective charge transfer in one of the stages is insignificant is of considerable interest. When the adsorption of the oxidised form is not accompanied by an appreciable charge transfer, i.e. when

$$\xi \ll 1;\ n_2 \simeq n\ , \qquad (21)$$

we have

$$Z_F = R_{22} + \frac{\widetilde{W}_{22}}{\sqrt{j\omega}} + \frac{1}{j\omega C_{22} + [R_{11}\xi^2 + \widetilde{W}_{11}\xi^2/\sqrt{j\omega}]^{-1}}\ , \qquad (22)$$

where $R_{11}\xi^2 = RT/(nF)^2V_{10}$ and $\widetilde{W}_{11}\xi^2 = RT/(nF)^2c_{10}\sqrt{D_1}$. Similarly, when charge transfer occurs predominantly in the stage involving the adsorption of the oxidised form, then

$$\xi \gg 1;\ n_1 \simeq n, \qquad (23)$$

and

$$Z_F = R_{11} + \frac{\widetilde{W}_{11}}{\sqrt{j\omega}} + \frac{1}{j\omega C_{11} + [pR_{11} + r\widetilde{W}_{11}/\sqrt{j\omega}]^{-1}}\ , \qquad (24)$$

where $pR_{11} = RT/(nF)^2V_{20}$ and $r\widetilde{W}_{11} = RT/(nF)^2c_{20}\sqrt{D_2}$. Eqns. (22) and (24) both correspond to the same equivalent circuit (Fig. 1*e*).

The results can be used to analyse the electrode reaction on platinum in the iodine–iodide system. The impedance of this system has been investigated[49–52]. Vetter[49] and Tyagai et al.[52] concluded that the electrode reaction proceeds via the discharge–recombination mechanism, the discharge stage being slow. Llopis et al.[50] showed that the experimental data correspond to the equivalent circuit in Fig. 1*e*. The hodograph of the input impedance of the cell is of the form shown in Fig. 3. Dane et al.[51] found the exchange current of the electrochemical reaction from the impedance data assuming that the resistance R_D is equal to the diameter of the half-circle shown in Fig. 3 by a dashed line and that $i_0 = RT/FR_D$. The study of the variation of i_0 with the concentration of I^- ions and of dissolved iodine led the authors[51] to the conclusion that the reaction proceeds via the discharge–electrochemical desorption mechanism. This view was confirmed by other methods and it was shown that the exchange currents are comparable for both stages[53].

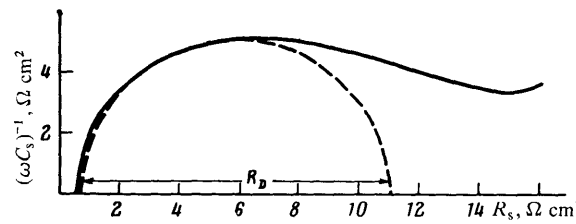

Figure 3. The hodograph of the impedance of the Pt/(1 *N* H_2SO_4 + 3.5 × 10^{-5} mole cm^{-3} KI + 0.46 × 10^{-6} mole cm^{-3} I_2) boundary at 25 °C (data of Llopis et al.[50]); impedance parameters: $R_e = 0.7\ \Omega\,cm^2$, $R_1 = 9.8\ \Omega\,cm^2$, $R_2 = 3.5\ \Omega\,cm^2$, $W_1 = 0$, $W_2 = 95.5\ \Omega\,cm^2s^{-1/2}$, $C_d = 3\ \mu F$ cm^{-2}, $C_2 = 31\ \mu F\ cm^{-2}$. The diameter of the dashed half-circle is approximately 10.2 Ω cm^2.

Parameters of the electrode impedance of the I_2/AgI system[54].

t, °C	C_d, μF cm^{-2}	C_2, μF cm^{-2}	R_1, Ω cm^2	R_2, Ω cm^2	W_1, Ω $cm^2s^{-1/2}$	W_2, Ω $cm^2s^{-1/2}$
197	46.3	15.9	0.10	0	98	2160
363	58.0	17.6	0.19	0	210	1180
498	64.5	20.8	0.20	0	130	590
549	79.6	21.5	0.20	0	92	325
618 (melt)	102	—	0.045	0	63	—

As shown previously[21], the discharge–recombination and discharge–electrochemical desorption mechanisms lead to the same a.c. current (Fig. 1*d*). If the diffusion of I^- ions does not make an appreciable contribution to the impedance (a fairly concentrated solution) and the discharge is transferred preferentially in the first stage so that $n_2 \simeq 0$ and $n_1 \simeq 2$, then the circuit in Fig. 1*d* transforms into that in Fig. 1*e*, for which $ZW_1 = 0$. The rates of the two adsorption stages, characterised by the resistance R_1 and R_2, are comparable (Fig. 3), which agrees with the results

of Povarov et al.[53]. Thus the experimental data of different workers for the impedance of the Pt/I_2, KI, H_2SO_4 boundary can be explained from the same standpoint using Eqn. (24). The C, I_2/α-AgI boundary with a solid electrolyte behaves similarly[54]. The equivalent circuit of the Faraday process in such a system is the same as in Fig. 1*d*. The impedance parameters are listed in the Table. In this case both the diffusion of I^- ions proceeding via the lattice defects and the diffusion of molecular iodine are significant. The impedance ZW_2 corresponds to the former and ZW_1 corresponds to the latter. This follows from the fact that, when the crystal melts, the impedance ZW_2 falls to zero, since all the I^- ions begin to participate in the transport.

IV. IMPEDANCE OF NON-EQUILIBRIUM ELECTROCHEMICAL SYSTEMS

The study of the properties of the electrochemical impedance of complex systems showed that it is necessary to use the principles of non-equilibrium thermodynamics and particularly the Onsager reciprocal relations. It was found that the dynamic adsorption equation for an irreversible electrode can be obtained from the Onsager relations and the adsorption equation for a reversible electrode[53]. In fact, for an ideally reversible electrode one can write the Gibbs adsorption equation:

$$-d\gamma = \Gamma_1 d\mu_1 + \Gamma_2 d\mu_2. \qquad (25)$$

The chemical potentials of the oxidised and reduced forms can be expressed in terms of the electrochemical ($\tilde{\mu}$) and the electrical (φ) potentials, i.e.

$$-d\gamma = \Gamma_1 d(\tilde{\mu}_1 + z_1 F\varphi) + \Gamma_2 d(\tilde{\mu}_2 + z_2 F\varphi). \qquad (26)$$

If the adsorbed species are in equilibrium with the adsorption layer, then we have for the reaction mechanism corresponding to Fig. 2*e*

$$-d\gamma = \Gamma_1 d(\tilde{\mu}_a + z_1 F\varphi) + \Gamma_2 d(\tilde{\mu}_a + z_2 F\varphi), \qquad (27)$$

$\tilde{\mu}_a$ being the electrochemical potential of the adsorbed species and z_1 and z_2 their charges. It follows directly from Eqn. (27) that[21]

$$-d\gamma = \Gamma_1 d\mu_1 + \Gamma_2 d\mu_2 + Q' d\eta_1 + Q' d\eta_2, \qquad (28)$$

where Q' and Q'' are the total thermodynamic charges on the electrode[56] and η_1 and η_2 are the overvoltages in the first and second adsorption stages.

The equation was obtained in relation to equilibrium conditions, but it is valid also for non-equilibrium electrodes (i.e. when a direct current is imposed), provided that the following two conditions are fulfilled: (a) when a direct current flows, the mechanism of the electrode process does not change; (b) the processes in the surface layer are fairly rapid, so that the thermodynamic properties of this layer are determined unambiguously by the electrode potential and the electrochemical potentials of the adsorbed species. In other words it is assumed that, regardless of whether there is an equilibrium between the surface and bulk-phase states, the state of the surface layer remains the same function of its surface variables.

If the electrochemical system in the absence of an alternating current does not correspond to equilibrium, for example when a direct current is imposed, the Onsager relations cease to hold although the Faraday process can still be represented by the equivalent multiterminal network. The overall impedance of the electrochemical reaction proceeding via the adsorbed state is in this case given by

$$Z_F = \frac{Z_{11}Z_{22} - Z_{12}Z_{21}}{(Z_{11} + Z_{22}) - (Z_{12} + Z_{21})}, \qquad (29)$$

where $Z_{12} \neq Z_{21}$. Formally the impedance Z_F can also be represented by a rational-fractional function of $(j\omega)^{-1/2}$ in which the numerator is a third-degree polynominal and the denominator is a second-degree polynomial. Thus the frequency variation of the impedance does not depend on the degree of reversibility of the system in terms of a direct current, but is determined exclusively by the mechanism of the electrochemical process. The coefficients of the rational-fractional function can vary with the degree of polarisation under a direct current. This relation can be determined on the basis of a specific reaction model.

In view of the inequality of Z_{12} and Z_{21}, the equivalent a.c. circuit of the type shown in Fig. 1*d* should include a dependent current source (see, for example, Atabekov[57]). Thus aperiodic equivalent circuits, analogous to those proposed by Barker[58,59] for reversible systems, can be constructed for irreversible systems.

The development of the theory of electrochemical impedance leads to great possibilities for the application of alternating currents in electrochemical kinetics to the study of complex reactions accompanied by adsorption both near equilibrium and following the imposition of a direct current.

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The Fundamental Step in Electrode Reactions

R.R.Dogonadze and L.I.Krishtalik

The modern quantum-mechanical theory of the fundamental step in electrode reactions, which takes into account the necessity for the reorganisation of the polar medium and the qualitative difference between the behaviour of classical and quantum-mechanical degrees of freedom, is briefly reviewed. The experimental studies on the influence of various factors on the pre-exponential factor, the kinetic isotope effect, and the activation energy for the evolution of hydrogen have demonstrated a satisfactory agreement with the predictions of the quantum theory and a qualitative contradiction with the Horiuti-Polanyi model, which postulates the extension of the O-H bond in the activation process.
The bibliography includes 50 references.

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I. INTRODUCTION

Reviews dealing with the theory of the fundamental step in electrode reactions[1] and certain experimental studies in this field[2] were published ten years ago in the issue of this journal devoted to the 70th birthday of Academician A. N. Frumkin. Since then the problem as a whole has developed very significantly, new ideas have been put forward, justified theoretically, and proved experimentally. In principle, these have permitted a theoretical analysis of any complex reaction involving charge transfer becoming possible.

II. THE QUANTUM THEORY OF THE FUNDAMENTAL STEP IN ELECTRODE REACTIONS

At the beginning of the 1960s only the simplest electron transfer reactions, unaccompanied by the dissociation, formation, or rearrangement of covalent bonds, could be treated theoretically. These studies revealed the decisive role of the reorganisation of the polar medium, i.e. the reorientation of the solvent dipoles in the course of such reactions. Electron transfer takes place after the molecules of the medium have attained a configuration (intermediate between the equilibrium initial and final configurations) as a result of thermal fluctuations for which the energies of the initial and final states are equal. These ideas were then extended to any charge-transfer reaction in the course of which not only the medium but also the reactants undergo rearrangement.

The principal ideas in the quantum chemistry of the fundamental step of electrochemical reactions will be described using as an example the discharge of hydrogen ions. This reaction was chosen, firstly, because it is apparently one of the electrochemical processes which have been investigated in greatest detail and, secondly, this reaction constitutes the simplest instance where the fundamental step involves the dissociation of a single covalent bond and the formation of another covalent bond. Finally, as will be seen below, the difference between the quantum theory and the theory of absolute reaction rates in relation to the mechanism of the fundamental step is manifested most clearly in proton transfer processes.

One of the first microscopic models used to describe the fundamental step in the electrochemical proton transfer process was proposed by Horiuti and Polanyi[3]. This study played a major role in the development of the theory of the kinetics of the fundamental step in chemical reactions, since it explained correctly for the first time a number of phenomenological relations. According to this theory, the proton is transferred from the AH^+ species to the electrode via a gradual extension of the $A-H^+$ bond, which corresponds to the excitation of the high vibrational levels in the AH^+ molecule. Subsequently, in order to account for the isotope effect, it was suggested that some tunnelling can occur near the top of the barrier (see, for example, Bell's review[4]). It is important to emphasise that, both in the initial study by Horiuti and Polanyi and in subsequent investigations based on the ideas of the theory of absolute reaction rates, the dynamic role of the polar medium in the fundamental step was completely ignored.

Dogonadze and coworkers[5,6] made the first attempt to consider proton transfer, within the framework of an extremely simplified model, on the basis of a fully quantum-mechanical calculation without any *a priori* hypothesis concerning the reaction pathway on the potential energy surface. Subsequently it was possible to improve significantly, on the one hand, the quantitative model used to describe the polar medium[7-9] and, on the other hand, to examine a more realistic model of the ion undergoing discharge, taking into account the possible changes in the intramolecular configurations of the reactants[10]. The method for calculating the rate of the fundamental step developed in these studies was in principle applicable not only to proton transfer reactions but to reactions of virtually any type. The modern quantum theory of chemical and electrochemical reactions in a condensed phase has been reviewed[11-15]. In the present survey we shall describe only some results of this theory and shall discuss qualitatively the overall features of the fundamental step.

In chemical kinetics the mechanism of the fundamental reaction step is usually treated with the aid of the potential energy surfaces of the initial state $U_i(Q)$ and the final state $U_f(\zeta)$. Here we denote by the symbol Q the entire set of coordinates of the degrees of freedom which are altered in the course of the reaction, and exert a dynamic influence on the fundamental step. Thus Q includes the set of coordinates R defining the configuration of the molecule (dipoles) of the medium and the set of coordinates r defining the intramolecular configuration of the reactants.

Quantum-mechanical calculation has shown (see, for example, Dogonadze and Kuznetsov[14]) that the probability of the transition per unit time from the initial potential energy surface $U_i(Q)$ to the potential energy surface of the final state $U_f(Q)$ can be formulated as follows†:

$$w_{if} = \text{const} \cdot L_{if}(Q^*) \cdot \Phi_i(Q^*, 1-\Theta^*) \cdot \Phi_f(Q^*, \Theta^*), \quad (1)$$

where $\Phi_i(Q, 1-\Theta)$ is the quantum-statistical distribution function for the coordinates in the initial state calculated for an effective temperature $T/(1-\Theta)$, $\Phi_f(Q,\Theta)$ is similarly the distribution function for the coordinates in the final state calculated for a temperature T/Θ, Θ is an auxiliary variable the physical significance of which will be explained below, $2L_{if}$ is the resonance splitting of the U_i and U_f surfaces in the vicinity of their intersection and is determined by the electronic exchange integral, Q^* are the coordinates of the "transition" configuration, and Θ^* is the value of Θ in the transition state; it is identical with α—the transfer coefficient or the symmetry factor in the Brønsted relation.

The transition configuration Q^* and the transfer coefficient Θ^* are determined in the following way according to the quantum theory[10,11]. For a fixed arbitrary value of Θ, we initially seek a maximum in the function $L_{if}(Q)\cdot\Phi_i(Q, 1-\Theta)\cdot\Phi_f(Q,\Theta)$ with respect to Q; then, having found $Q^*(\Theta)$, we determine Θ^* from the condition for the maximum in the function $L_{if}[Q^*(\Theta)]\cdot\Phi_i[Q^*(\Theta), 1-\Theta]\cdot\Phi_f[Q^*(\Theta), \Theta]$ with respect to Θ. Having found Θ^*, we find the transition configuration $Q^* = Q^*(\Theta^*)$.

The formula of the theory of absolute reaction rates can be easily found from Eqn. (1). For this purpose, it is sufficient to suppose that motion is classical for all degrees of freedom. Then the classical Boltzmann distribution function[19,20] should be used as the distribution function with respect to coordinates:

$$w_{if}^{cl} = \text{const} \cdot L_{if}(Q^*) \cdot \exp\left[-(1-\Theta^*)\frac{U_i(Q^*)}{kT} - \Theta^*\frac{U_f(Q^*)}{kT}\right]. \quad (2)$$

The system of equations for Q^* and Θ becomes under these conditions

$$(1-\Theta)\frac{\partial U_i(Q)}{\partial Q_k} + \Theta\frac{\partial U_f(Q)}{\partial Q_k} = kT\frac{\partial \ln L_{if}(Q)}{\partial Q_k}, \quad (3)$$

$$U_i[Q^*(\Theta)] = U_f[Q^*(\Theta)]. \quad (3')$$

Condition (3′) implies that the transition from the surface U_i to U_f proceeds via the intersection surface, where U_i is equal to U_f. This condition corresponds fully to the classical features of the transition adopted in the theory of absolute reaction rates.

In analysing Eqn. (3), one should bear in mind that the exchange integral L_{if} depends virtually only on the intermolecular coordinates R of the reactants. For this reason, in determining the transition configuration with respect to the intramolecular coordinates r^* and the coordinates of the molecules of the medium q^*, the right-hand side of Eqn. (3) can be replaced by zero. In other words, for fixed intermolecular coordinates R of the transition configuration, a saddle point on the surface of intersection of U_i and U_f corresponds to r^* and q^*. Eqn. (3) for the coordinates R^* makes it possible to find the optimum distance between the reactants and their optimum mutual orientation. The existence of this optimum is a consequence of the fact that L_{if} decreases sharply with increase of the distance between the reactants, while for short distances the probability of the mutual approach of the reactants $e^{-U_i/kT}$ diminishes sharply.

Taking into account condition (3′), formula (2) can be rewritten as follows:

$$w_{if} = \text{const}\, L_{if}(Q^*)\exp\left[-\frac{U_i(Q^*)}{kT}\right]. \quad (4)$$

Here $U_i(Q^*)$ plays the role of activation energy and const. contains a number of factors which determine the transmission coefficient and the frequencies of the fluctuations leading to the formation of the transition state (the entropy term).

Together with the classical limit, which formally occurs when sufficiently high temperatures ($T \to \infty$) are considered, it is of interest to examine the opposite limiting case of low temperatures ($T \to 0$). Here the behaviour of the system is determined by purely quantum-mechanical factors and the distribution function for the coordinates is equal to the square of the modulus of the wave function for the system in the ground state Ψ_0.[19,20] Above we pointed out the formal criterion for the classical ($T \to \infty$) and quantum-mechanical ($T \to 0$) behaviour of the system. In order to obtain the real quantitative criterion in terms of temperature, we shall consider the case, which is of practical interest, where the system is described by a set of harmonically vibrating oscillators. Denoting by $Q_k^{(i)}$ and $\omega_k^{(i)}$ the normal coordinates and frequencies in the initial state and by $Q_k^{(f)}$ and $\omega_k^{(j)}$ the normal coordinates and frequencies in the final state, Eqn. (1) can be rewritten as follows[19]:

$$w_{if} = \text{const}\, L_{if}(Q^*)\prod^{k}\exp\left[-(Q_k^{*(i)})^2\tanh\frac{\hbar\omega_k^{(i)}(1-\Theta^*)}{2kT} - (Q_k^{*(f)})^2\tanh\frac{\hbar\omega_k^{(f)}\Theta^*}{2kT}\right]. \quad (5)$$

Eqn. (5) becomes identical with Eqn. (2), corresponding to the classical limit, when all the hyperbolic tangents are replaced by their arguments, which is possible for arguments much smaller than unity. Thus we arrive at the following criterion of classical behaviour of the system‡:

$$\hbar\omega_k^{(i)}(1-\Theta^*) \ll 2kT, \qquad \hbar\omega_k^{(f)}\Theta^* \ll 2kT. \quad (6)$$

Since the transfer coefficient $\alpha = \Theta^*$ lies in the range zero to unity[2,11,13], it is sufficient for classical behaviour of the system that the energy of the vibrational quantum $\hbar\omega$ should be small compared with the energy of thermal motion $2kT$.

We shall use criterion (6) to elucidate the problem of the quantum-mechanical or classical behaviour of the proton in chemical and electrochemical reactions. We shall assume initially that the reaction proceeds in the normal region of thermal excitation where $\alpha \simeq 0.5$. According to condition (6), the parameter $\gamma \simeq \hbar\omega/4kT$ should be estimated in this case. If $\omega \simeq 6\times10^{14}$ s^{-1} is adopted as the vibrational frequency, then we obtain $\gamma \simeq 3.75$ at room temperature. Since $\tanh 3.7 \simeq 0.999 \simeq 1$, we obtain the

† Eqn. (1) is valid for non-adiabatic processes when the transmission coefficient κ is less than unity. Adiabatic processes have been examined in a number of studies[16-18]. Since $\kappa \ll 1$ for proton transfer reactions, as shown by studies on the isotope effect, in the present review we shall consider only non-adiabatic reactions.

‡ Together with condition (6), another condition, namely the requirement that the subsequent terms of the expansion of the tangent be small, follows from Eqn. (5). It has been shown[10] that this condition does not usually alter significantly Eqn. (6).

following distribution function for the coordinates of the proton:

$$\Phi(Q) = \frac{1}{\sqrt{\pi}} e^{-Q^2} \equiv |\Psi_0(Q)|^2, \quad (7)$$

where $\Psi(Q)$ is the wave function of the ground vibrational state of the proton. Thus the distribution function of the proton coordinates at room temperature is determined by purely quantum-mechanical laws. In particular, the coordinates $Q > 1$, which are located in the inaccessible region according to the classical theory, can be realised only by virtue of the tunnel effect. Finally, we may note that, according to Eqn. (7), the distribution function for the proton coordinates is independent of temperature, like that for any quantum-mechanical particle.

We shall now consider the region of barrierless reactions, i.e. highly endothermic processes [2,11-15]. In this case the transfer coefficient Θ^* is close to unity and, according to condition (6), when $\hbar\omega(1-\Theta^*) \ll 2kT$, the behaviour of the proton in the initial state is classical. The physical significance of this result is that in highly endothermic processes a preliminary excitation of the proton to a high vibrational level, where its behaviour becomes virtually classical, is necessary. In particular, one may say that, in the formation of the transition state, the chemical bond involving the proton undergoes classical "extension". Evidently [this also follows from formula (6) according to which $\hbar\omega\mathfrak{G}^* \gg 2kT$ for the proton in the barrierless region], after the rearrangement of the electronic state in the transition region, the proton is in the vibrational ground state. In this sense, one may say that the classical degree of freedom of the proton is converted into the quantum-mechanical degree of freedom in the course of the reaction. A completely analogous treatment has shown that, in reactions without activation energy, i.e. in highly exothermic processes, where Θ^* is close to zero, the proton passes from its ground vibrational state to a highly excited vibrational state.

One must emphasise that the conclusion concerning the virtually classical behaviour of the proton in a barrierless discharge is valid only for very high activation energies, i.e. far from the region of transition from normal discharge to barrierless discharge. The existing theory, which provides a qualitatively correct explanation of the variation of α from 1/2 to 1, does not describe the transition region quantitatively. In particular, it is not yet been possible to account for the expérimental observation of a sharp variation of α over a very narrow range of potentials [2]. Certain estimates, carried out using Morse potentials, have shown that in the transition region the lowest excited levels of the proton make an appreciable contribution together with its ground vibrational level, but the behaviour of protons still remains significantly of the quantum-mechanical type [11].

The scheme described above leads to the following physical picture of the transition from the initial to the final state. On the potential energy surface for the initial state, a classical fluctuation takes place initially in accordance with the Boltzmann Law along the degrees of freedom for which the first condition (6) holds. The extension of the length of these classical degrees of freedom depends significantly on the behaviour of the given degree of freedom after the reaction: if it remains classical also after the reaction, the transition configuration is determined by Eqn. (3), but, when there is a change from a classical to a quantum-mechanical (quantised) degree of freedom as a result of the reaction, the extension is virtually a maximum, since in the final state the system must be at the zero-point level, i.e. must be localised near the equilibrium configuration of the final state.

As a result of the classical fluctuation, all the zero-point (ground) energy levels of the quantum-mechanical subsystem, satisfying conditions which are the opposite of conditions (6) in both the initial and final states, are equalised in the initial stage. In fact we are dealing here with the general Franck–Condon principle, according to which the rearrangement of the state of the fast subsystem (in our case the quantum-mechanical subsystem) can occur only when the energies of the initial and final states are equal, since the slow subsystem (in our case the classical subsystem) cannot change (because of the considerable inertia) its coordinates and momenta, in order to compensate the difference between the energies of the fast subsystem.

In the second stage quantum fluctuation, i.e. tunnelling of the quantised degrees of freedom, begins for fixed coordinates of the classical subsystem. For a certain configuration of the quantised degrees of freedom, corresponding to the inaccessible region according to the classical theory, the energies of the initial and final states of the electronic subsystem are equalised. Thus at this stage the condition of the usual Franck–Condon principle is fulfilled; according to this principle, the change of state of the electronic (fast) system takes place for fixed coordinates and momenta of the nuclear (slow) subsystem. After the Franck–Condon barrier to the electronic subsystem is removed in the second stage, in the third stage there is electron tunnelling from the initial to the final state, after which there is an initial relaxation of the quantised and then the classical degrees of freedom of the system.

Cases are in principle possible (and probably extremely common) where the electronic subsystem follows adiabatically the motion of the remaining quantised subsystems, for example protons. In this case the second and third stages described above in fact merge into one and the only transition under the barrier is the one executed by the quantised subsystem of the nuclei. For such processes, which are adiabatic with respect to electrons and non-adiabatic with respect to other quantised degrees of freedom, L_{if} in Eqn. (1) can be understood as, for example, the proton exchange integral and no longer the electron exchange integral.

It is interesting to consider one of the characteristics of the reactions in the course of which a classical degree of freedom is converted into a quantised degree of freedom. If the conditions

$$\frac{2kT}{\hbar\omega^{(f)}} \ll \Theta^* \ll 1, \quad (8)$$

hold in the system, then the right-hand side of the inequality ensures that the reaction proceeds virtually without activation energy, while the left-hand side of the inequality implies that the given degree of freedom can be treated as virtually of the quantum-mechanical type in the final state (see Dogonadze et al.[6]). This implies that, although the process as a whole occurs almost without activation energy (in the sense that Θ^* is close to zero), it follows from the picture of the transition described above that there will be preliminary activation along the given degree of freedom from the initial equilibrium configuration to the final equilibrium configuration. Processes in which $\Theta^* \simeq 0$ but the activation energy is non-zero and constant (independent of the heat change) have come to be called quasi-non-activated processes. Quasi-barrierless processes, where $\mathfrak{G}^* \simeq 1$ but the activation energy differs from the heat change by a constant amount, can be treated similarly [21,22].

On passing from simple potential energy surfaces, having the form of multi-dimensional paraboloids, to more complex surfaces, the qualitative picture of the transition naturally does not change. Only the form of the criterion of the quantum-mechanical or classical behaviour of the given degree of freedom is altered: instead of condition (6), we have a more complex condition. The new feature introduced into the qualitative picture by the anharmonicity of the potential energy curves is that, along different sections of the potential energy curve, there can be a change from the classical to the quantum-mechanical (tunnel) motion of the particle or conversely. For example, when the vibrational frequency near the minimum satisfies the condition of classical behaviour ($h\omega \ll 2kT$), the behaviour of the system far from the minimum can be nevertheless of the quantum-mechanical type if the potential energy curve rises very steeply in consequence of the marked repulsion from another particle. The opposite situation can also arise when the vibrational frequency near the minimum satisfies the condition for quantum-mechanical behaviour ($h\omega \gg 2kT$) and yet the motion of the particle is classical at a sufficient remove from the minimum where the potential energy curve acquires a low slope.

However, one should remember that the motion of the particle becomes classical in a state very close to dissociation. For example, numerical calculation of the quantum-statistical distribution function for the proton coordinates using the Morse potential curve with the parameters D (dissociation energy) = 172.5 kcal mole^{-1} and ω (frequency near the minimum) = 4×10^{14} s^{-1} has shown that the motion of the proton becomes classical when it departs from the minimum by a distance of about 4 Å. Such extension of the bond requires an energy consumption of the order of 100 kcal mole^{-1}, i.e. much greater than the experimental activation energies (< 20 kcal mole^{-1}). Therefore under real experimental conditions the classical behaviour of the proton in the highest state is unlikely.

III. EXPERIMENTAL STUDY OF THE FUNDAMENTAL STEP IN ELECTRODE REACTIONS

We shall consider the possibility of an experimental comparison of two fundamentally different models of the fundamental step in the discharge of a proton donor—the model involving a gradual extension of the O–H bond and the model postulating a rearrangement of the solvent structure with a subsequent quantum jump of the proton from the initial to the final state. Both give virtually the same explanations of the majority of the known experimental facts. This is not surprising, since, for a semi-quantitative treatment of the majority of observations, it is sufficient that certain simple phenomenological relations, associated with the existence of an energy barrier, are maintained regardless of the causes responsible for the barrier. Therefore, in order to choose between the two models, it is necessary to seek relations for which they would give rise to qualitatively different predictions.

The first group of phenomena for which significant differences between the conclusions reached on the basis of the two theories may be expected is associated with the pre-exponential factor, namely with the influence on the latter of the probability of a tunnel transition of the proton through the barrier. The correction for tunnelling within the framework of the bond extension model has been estimated in a number of studies. Without going into their analysis, we may note the common and most significant feature of all these investigations—in this model tunnelling is determined by the same barrier as the activation energy—the barrier along the proton coordinate. On the other hand, within the framework of the quantum-mechanical theory, the activation energy is determined by the barrier on the classical coordinate, describing the orientation of the solvent dipoles, and the probability of the transition under the barrier is determined by the energy profile along the proton coordinate. Thus in the first model the activation energy and the pre-exponential factor are linked by a definite relation, while in the second model they can in principle vary independently.

The existence of barrierless electrode processes, in particular the barrierless discharge of the hydrogen ion, for which the activation energy is equal to the heat of the fundamental step (see Krishtalik's review [2]), was demonstrated previously. In the bond extension model the barrierless process involves the absence of a barrier on the path followed in the motion of the proton and hence the absence of a tunnell effect. The implication is that in this model κ for the barrierless discharge should be unity, while in the usual discharge $\kappa < 1$. In the quantum-mechanical model the energy profile along the solvent coordinate is barrierless, while the barrier along the proton coordinate is retained. Thus this theory leads to the conclusion that values of $\kappa < 1$ are of similar order of magnitude for both the barrierless and the usual discharges§.

Theoretical calculation of the pre-exponential factor, particularly for electrode processes, by the method of the theory of absolute reaction rates involves certain difficulties concerning the estimation of the entropy of the activated state [24,25]. However, for a barrierless discharge all these difficulties disappear, because here the activated state is identical with the final state. This permits a fairly rigorous calculation of the theoretical value of the pre-exponential factor for the barrierless discharge [26]. The theoretical value $\lg k = 5.7$ (the pre-exponential factor k is expressed in A cm^{-2}) is much higher than the experimental value $\lg k = 3.0$. This discrepancy indicates a significantly non-adiabatic process ($\kappa = 10^{-2.7}$), i.e. a fairly low probability of proton transfer below the barrier. As shown above, $\kappa \ll 1$ for a barrierless discharge can be hardly explained by assuming that the extension of the O–H bond determines the activation process, but it can be naturally accounted for within the framework of the quantum-mechanical theory.

A similar conclusion can be reached also by comparing the pre-exponential factors for the barrierless and the usual discharges. In order to compare the tunnelling probabilities, it is necessary to compare ideal rather than real pre-exponential factors, i.e. a correction must be introduced for the change in the entropy of the electrode process and account must be taken of the concentration dependence of the pre-exponential factor. Such a calculation has been made [27] and showed that the tunnelling probabilities for the barrierless and the usual discharges are similar (the difference between them is within the

§ Since the experiments are performed at potentials close to the transition region, the possibility of a change from the quantum-mechanical to the classical motion of the proton discussed above need not as yet be taken into account here. The involvement of the first excited vibrational levels in the barrierless process together with the ground level can lead to an increase of κ.

limits of experimental error). This result also agrees with the quantum-mechanical theory, but is difficult to explain on the basis of the bond extension model.

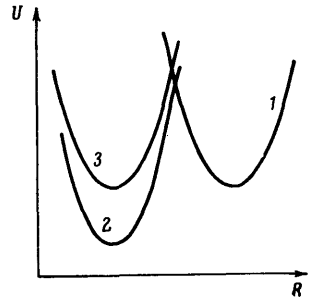

Figure 1. Schematic potential energy curves: 1) component describing the O–H bond; 2) and 3) components describing the M–H bond ($E_{M_2} > E_{M_3}$).

We shall consider the influence of the nature of the metal on the probability of proton tunnelling[28]. From the standpoint of the bond extension model (Fig. 1), the higher the energy of the M–H bond ($E_{M\text{-}H}$) the lower the height of the barrier for tunnelling and the narrower the barrier (the potential curve rises more steeply for a more rigid bond). Consequently Fig. 1 leads to the conclusion that tunnelling by the proton is facilitated by higher values of $E_{M\text{-}H}$. In the quantum-mechanical model the probability of the transition below the barrier increases with increased overlap of the wave functions of the proton in the initial and final states. The more rigid the bond the more highly localised the proton and the less effective the overlapping of the wave functions (Fig. 2). Therefore, within the framework of the given model, one may expect a decrease of tunnelling probability with increase of $E_{M\text{-}H}$. Fig. 3 shows that experiment agrees with this conclusion.

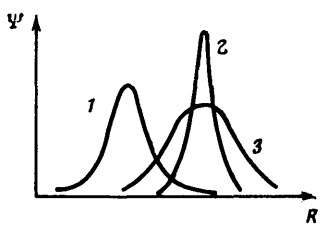

Figure 2. Wave functions of the proton in OH (curve *1*) and MH (curves *2* and *3*) ($E_{M_2} > E_{M_3}$).

The probability of tunnelling by the proton influences significantly another quantity susceptible to measurement—the isotope separation factor S. The experimental value is determined by kinetic isotope effects for two irreversible stages—discharge (S_d) and electrochemical desorption (S_{ed})[35,36]:

$$S = \frac{2S_dS_{ed}}{S_d + S_{ed}}. \qquad (9)$$

Electrochemical desorption on mercury and similar cathodes is highly exothermic, so that its activation energy should become zero[2,22,37].¶ If the activation process consists of the extension of the bond, then the non-activated electrochemical desorption should proceed at the same rate for all hydrogen isotopes, since there is no barrier to tunnelling by the proton and since, by virtue of the zero activation energy, the effect of the difference between the zero-point energies disappears. In other words, in this model $S_{ed} = 1$. But this implies that $S = 2S_d/(S_d + 1) \leqslant 2$. This conclusion is completely inconsistent with experimental data—as will be shown below, fairly large effects can be observed on mercury and similar metals ($S_{H/T}$ varies from 3 to 17). On the other hand, in the new quantum-mechanical theory this difficulty does not arise, because the non-activated process is associated solely with the absence of a barrier on the coordinate for the solvent dipoles, while the barrier persists along the proton coordinate[28].

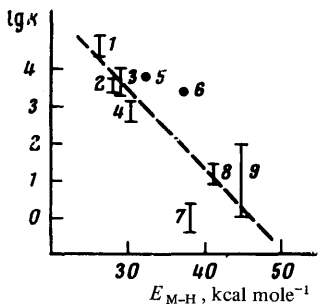

Figure 3. Variation of the pre-exponential factor for the hydrogen evolution reaction in acid solutions with the M–H bond energy: 1) 40.6 at.% thallium amalgam[29]; 2) lead[30]; 3) mercury[25,26,31]; 4) 60.3 at.% indium amalgam[32]; 5) gallium–16.4 at.% indium[31]; 6) gallium[31]; 7) silver (0.1 *N* HCl)[33]; 8) silver (0.1 *N* H_2SO_4);[33] 9) indium[34].

Within the framework of the bond extension model, the metal of the cathode influences S mainly because of its influence on the isotope effect at the discharge stage, since it affects S_{ed} much less (and in non-activated desorption not at all). If one considers the nature of the overlap of the proton wave functions in the initial and final states, it is seen that the change in the M–H bond energy acts in the same direction on tunnelling probability both in the discharge and in electrochemical desorption, i.e. both on S_d and on S_{ed}. The influence of the nature of the metal on tunnelling probability was considered above from the standpoint of both the models discussed. In agreement with the quantum-mechanical model and the experimental pre-exponential factors for the reaction, it was found[28] that an increase of the M–H bond energy, which hinders proton transfer under the barrier, increases the kinetic isotope effect.

¶ The conclusion that the electrochemical desorption of hydrogen from metals of the same type as mercury proceeds without activation energy is confirmed by the results of Rotenberg, Pleskov, and coworkers[38] (see below).

Experimental data indicate a significant lowering of the isotope separation factor with increase of the potential[28,39]. Within the framework of the bond extension model, this type of relation can be explained by a decrease of the activation barrier with increase of the potential and, accordingly, by the facilitation of tunnelling by the proton[40]. The new theory leads to the conclusion that there is no direct relation between the activation energy (barrier on the coordinate of the solvent dipoles) and the probability of proton tunnelling. The decrease of S with increase of the potential can be explained from this standpoint by the larger overlap of the wave functions for the initial and final states because of the approach of the hydronium ion to the electrode under the influence of the electric field. The validity of this explanation is evident from a comparison of the isotope effects in acid and alkaline solutions. In the latter the uncharged water molecule, which is naturally attracted to the electrode much less strongly than the H_3O^+ ion, serves as the proton donor. Its distance from the electrode hardly changes with potential and therefore there is no dependence of the isotope effect on the potential (Fig. 4).[28,41]

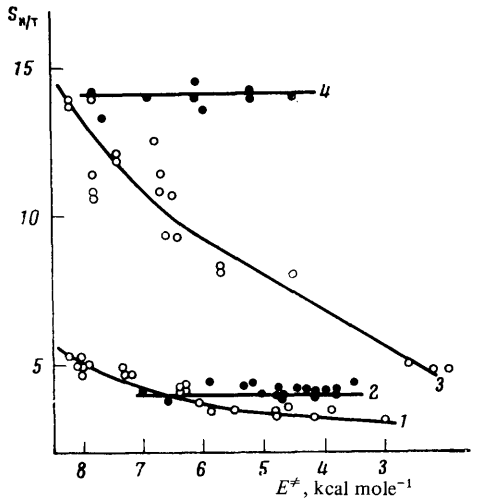

Figure 4. Variation of the separation factor for protium (H) and tritium (T) with activation energy: 1) mercury, acid[28,42]; 2) mercury, alkali[28,42]; 3) gallium, acid[28,41]; 4) gallium, alkali[41].

From the standpoint of the O–H bond extension model, there is no fundamental difference between the discharge of H_3O^+ and H_2O—in both cases the potential barrier is lowered with increase of the overvoltage and facilitation of tunnelling is to be expected. Fig. 4 shows that, for the same activation energies in acid and alkaline solutions, there is a significant difference between the variation of S with potential. This shows that, in full agreement with the new quantum-mechanical theory, there is no direct relation between the activation energy and the probability of tunnelling by the proton†.

The above explanation of the variation of S with potential presupposes that, with increase of the electric field, the pre-exponential factor for the discharge of the hydrogen ion should increase. In the study of the temperature dependence of the rate of this reaction over the usual, fairly narrow range of potentials this effect lies at the limit of experimental error (a weak tendency to change has been observed[31]), but it has been shown[44] that, on a silver cathode for potentials in the region of 1 V, the pre-exponential factor increases at least by two orders of magnitude.

The much weaker attraction of water molecules to the electrode compared with the H_3O^+ ion must result in a greater distance between the initial and final positions of the proton and hence in a smaller tunnelling probability. This conclusion has been fully confirmed experimentally—the ratio of the tunnelling probabilities for H_3O^+ and H_2O, found from the pre-exponential factors, is $10^{5.6}$ for gallium and $10^{4.8}$ for the indium–gallium alloy[31].

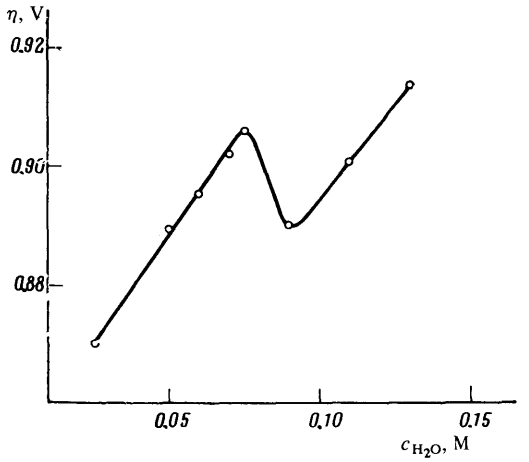

Figure 5. Variation of the hydrogen overvoltage (for $\log i = -4.0$) in 0.01 N $HClO_4$ solution in acetonitrile with the concentration of water.

Another approach to the study of the mechanism of the fundamental step in hydrogen evolution consists of employing a medium with properties significantly different from those of water. We chose the aprotic weakly basic solvent

† Christov[43] drew attention to the fact that, for certain parameters of the barrier on the proton coordinate, the optimum region for tunnelling is located at some distance from the top of the barrier, so that the tunnelling probability is independent of activation energy. This factor might explain, within the framework of the bond extension model, the constancy of S in alkaline solutions, but, on the one hand, there is no evidence that the real parameters of the barrier correspond to conditions necessary for this and, on the other hand, even with the aid of these additional hypotheses it is still impossible to account for the above data concerning the barrierless and non-activated processes and the influence of the nature of the cathode metal.

acetonitrile as a medium of this kind[45]. In anhydrous acetonitrile the hydrogen overvoltage of the mercury cathode in an acid solution is lower by about 150 mV than in water. After the addition of small amounts of water, which is a much stronger base than acetonitrile, hydronium ions are formed and the concentration of acetonitrilonium ions, which are the main proton donors, decreases. This leads to a corresponding increase of the overvoltage (Fig. 5). At a fairly high concentration of water the fraction of H^+ ions bound to the solvent becomes vanishingly small and hydronium ions become the main source of protons. From this instant, further addition of water decreases the overvoltage because the concentration of H^+ ions bound to water becomes virtually constant, while the concentration of the electrode reaction product (free water) increases. This results in a maximum on the curve in Fig. 5.

The hydronium ion can exist in acetonitrile both in the H_3O^+ form and as its association complex with one, two, or three water molecules (the last form predominates in aqueous solutions). Calculation based on Kolthoff and Chantooni's data[46] showed that, near the maximum on the curve in Fig. 5, the dominant species are $H_3O^+.H_2O$ and H_3O^+. This implies that the ion undergoing discharge is surrounded mainly by acetonitrile molecules. On the other hand, at a higher water concentration the fraction of $H_3O^+.2H_2O$ and $H_3O^+.3H_2O$ ions increases, i.e. the immediate coordination sphere of the H_3O^+ ion becomes increasingly similar to that in aqueous solution, which gives rise to a new increase of overvoltage. Although the mole fraction of water under these conditions is only 0.007 and the macroscopic properties of the medium have still not been able to change significantly, the micromedium near the hydronium ion becomes more "water-like" by virtue of the selective formation of hydrates and this has a significant influence on the kinetics of the discharge of the hydronium ion. Thus the influence of the change in the properties of the medium under the conditions of a virtually unchanged type of bond dissociation process are clearly manifested in these experiments.

Pre-exponential factors and activation energies.

Ion undergoing discharge	Medium	A_0, kcal mole^{-1}	lg k (A litre mole^{-1} cm^{-2})
CH_3CNH^+	CH_3CN	18.2	2.1
H_3O^+	CH_3CN	18.2	3.2
H_3O^+	H_2O	21.9	3.4

The influence of the medium and of the nature of the bond being ruptured is shown even more clearl y when the pre-exponential factors and the activation energies for the discharge of acetonitrilonium and hydronium ions are compared in acetonitrile and in water. All the pre-exponential factors in the Table have been recalculated for the same concentration of H^+ ions and for the same mole fraction of the conjugate base, which is unity (this correction, which is necessary to compare the data, was introduced for H_2O in the discharge of H_3O^+ in acetonitrile).

The Table shows that the discharge of the CH_3CNH^+ and H_3O^+ ions in acetonitrile solutions is characterised by significantly different pre-exponential factors and virtually the same activation energies, while the discharge of H_3O^+ in the two different media (water and acetonitrile) is characterised by virtually identical pre-exponential factors but different activation energies. Thus it has been found that the pre-exponential factor is determined mainly by the nature of the bond dissociated (N–H or O–H), while the activation energy depends on the solvent (acetonitrile or water). This conclusion is fully consistent with the predictions of the theory, according to which the activation energy is determined by the rearrangement of the structure of the medium and the pre-exponential factor is determined by the probability of tunnelling by the proton. On the other hand, from the standpoint of the bond-extension model, both the pre-exponential factor and the activation energy are determined by the bond undergoing dissociation, so that different relations are to be expected—similarity of the activation energies for the discharge of H_3O^+ ions in acetonitrile and water and different values of A_0 for the discharge of CH_3CNH^+ and H_3O^+ in acetonitrile. Thus different experimental data support a mechanism of proton transfer which relates the activation process only to a rearrangement of the structure of the medium without a significant extension of the bond between the proton and the proton donor.

Another aspect of the problem of the fundamental step in hydrogen evolution, which has been studied in the very last few years, is the nature of the rapid stage—the removal of adsorbed hydrogen. In their studies by the photoemission method Rotenberg, Pleskov, and coworkers[38] succeeded in determining the sum of the transfer coefficients for two reactions involving the removal of adsorbed hydrogen—electrochemical desorption and ionisation. For the mercury cathode in the range of potentials susceptible to investigation, it was found to be 0.5, which supported the hypothesis that one of the stages has no activation energy (most probably electrochemical desorption). On the other hand, for the bismuth cathode it was possible to attain potentials at which the above sum became zero, i.e. the possibility that both reactions can occur without activation energy was demonstrated.

Non-activated electrochemical desorption of hydrogen from metals of the same type as mercury was found to be fully irreversible (at least at overvoltages susceptible to measurement). This follows unambiguously from the isotope separation factor, which exceeds significantly the equilibrium constant for the isotope exchange between hydrogen and water[47].

The irreversibility of electrochemical desorption leads to the appearance of a new interesting phenomenon- a non-equilibrium ratio of the ortho- and para-modifications of hydrogen in the gas evolved on electrolysis at reduced temperatures[48,49]. A theory of this phenomenon was developed recently within the framework of the general quantum-mechanical theory of proton transfer[49].

In the hydrogen evolution reaction the species transferred (the proton) behaves significantly in accordance with the quantum-mechanical mechanism. Another situation arises in the transfer of heavy ions, linked by weaker bonds, i.e. their motion takes place in accordance with both the classical and quantum-mechanical mechanisms. As shown above, this feature of systems with heavy atoms leads to the occurrence of quasi-barrierless and quasi-non-activated processes characterised by $\alpha = 1$ and $\alpha = 0$ respectively. In this case the barrier disappears only for motion along the solvent coordinate, but remains on the heavy atom coordinate. However, the latter barrier does not change with the potential, so that α is determined only by the motion along the solvent coordinate.

The existence of quasi-barrierless processes was postulated previously for the chlorine evolution reaction on graphite and for the oxidation of azide on platinum [2]. The occurrence of quasi-barrierless and the reverse quasi-non-activated processes was recently demonstrated unambiguously for the evolution and ionisation of chlorine on ruthenium–titanium oxide anodes (RuO_2–TiO_2 solid solution). This process proceeds in stages:

$$Cl^- \overset{-e}{\rightleftarrows} Cl_{ad} \overset{-e}{\rightleftarrows} Cl^{+I} + Cl^- \rightleftarrows Cl_2.$$

The slow stage, involving the abstraction of the second electron, can be both of the usual type ($\alpha_a = 1/2$) and of the quasi-barrierless type ($\alpha_a = 1$), while in the opposite direction it is a quasi-non-activated process ($\alpha_c = 0$). If the slow stage were not of the quasi-barrierless type but simply of the barrierless type, i.e. if the abstraction of the second electron were not followed by the relaxation process involving a change in the heavy particle coordinate, then the second and third stages would have occurred as a single step and the reaction would have been of second order with respect to chloride ions. The experimental first order of the reaction demonstrates the quasi-barrierless nature of the electrode process [50].

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The Electrical Double Layer Capacitance and the Zero-charge Potentials of Metals in a Solid Electrolyte

S.V.Karpachev, I.D.Remez, V.V.Sal'nikov, and A.T.Filyaev

Studies of the properties of the electrical double layer and of the zero-charge points for certain metals in a solid electrolyte consisting of stabilised zirconium dioxide are reviewed. The influence of the electrode potential, temperature, and composition of the gas phase on the double layer capacitance and the zero-charge point is examined. A correspondence is established on the basis of experimental data between the potential of the minimum on the "capacitance-potential" curve and the zero-charge points for tin and silver.
The bibliography includes 16 references.

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I. INTRODUCTION

As a result of research by Frumkin and his school, the importance of studies of the structure of the electrical double layer and zero-charge potentials for electrochemical kinetics has now been demonstrated. In a study of the cathodic evolution of hydrogen from acid aqueous solutions Frumkin et al.[1] discovered the dependence of the overvoltage on the concentration of an extraneous electrolyte at a constant current density and acid concentration. They showed that this is due to the influence of the added neutral electrolyte on the double layer structure (on the ψ_1 potential). Furthermore, Frumkin showed[2] that in the cathodic reduction of complex anions the current decreases sharply until the attainment of the zero-charge potential owing to the increasing diffuseness of the double layer. This effect was established for several metals, the zero-charge potentials of which are appreciably different.

Electrochemical cells with an electrolyte consisting of stabilised zirconium dioxide have now acquired great practical importance and for this reason a more profound study of the electrochemical kinetics in solid electrolytes has become necessary; the investigation of the properties of the electrical double layer and of the zero-charge potentials of metals in the stabilised zirconium dioxide solid electrolyte has begun. The experimental data obtained for this new type of electrolyte are extremely interesting in the light of the theoretical ideas developed by Frumkin and his school.

II. EXPERIMENTAL DATA FOR THE STRUCTURE OF THE ELECTRICAL DOUBLE LAYER IN SOLID ELECTROLYTES

The first measurements of the double layer capacitance in the stabilised zirconium dioxide electrolyte were made by ourselves on a platinum wire electrode[3]. The dependence of the electrical double layer capacitance on potential is presented in Fig. 1. The capacitance–potential curves have a distinct minimum at a specific potential. The measurements were made at 1020°C in an electrolyte having the composition 85 mole % ZrO_2 + 15 mole % CaO in an atmosphere of argon freed from oxygen by being passed over metallic calcium at 650°C. All the measurements were performed at 10 kHz with the capacitance and resistance connected in series in one of the arms of an a.c. bridge. It was subsequently established that at 10 kHz there is still some dispersion of the capacitance and therefore the measured capacitance values involve an error; however, the type of the variation of the capacitance with potential is probably correct.

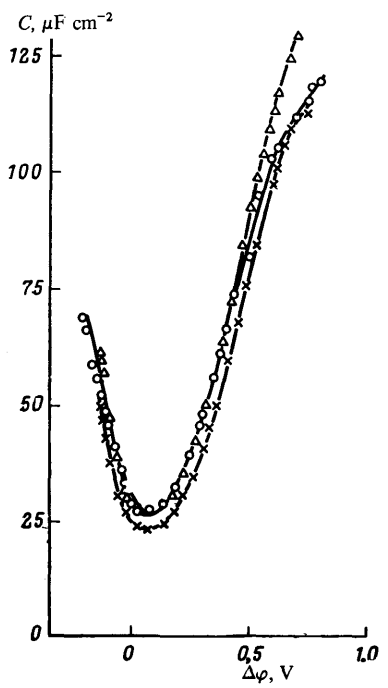

Figure 1. Variation of the differential electrical double layer capacitance with potential on a platinum electrode. The reproducibility of the results for three specimens is indicated.

We assumed that the dispersion of the capacitance at such comparatively high frequencies is due to the low value of the Faraday impedance caused by the high temperature. Hence it was necessary to carry out experiments at higher frequencies. Furthermore, it was desirable to employ as the test electrode a drop of fused metal rather than the solid metal. Evidently in this case the surface area of the junction between the electrode and the electrolyte, determined from geometrical dimensions, is closer to the true value.

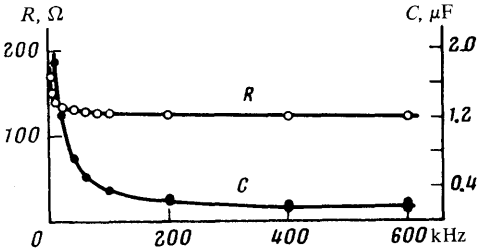

Figure 2. Variation of the capacitance and resistance with frequency.

The double layer capacitance was measured for liquid silver and tin drops at the equilibrium potential in the same electrolyte at 970°C in an atmosphere of purified argon[4]. The electrode potentials were determined with the aid of an electrochemical gas-analyser, which consisted[5] of a ceramic test-tube made of stabilised zirconium dioxide with platinum electrodes attached to its inner and outer surfaces. The test-tube was positioned so that the outer electrode was in the gas space of the electrochemical cell and the inner space of the test-tube communicated with the atmosphere. The potential difference arising in the electrochemical concentration cell between the platinum electrodes made it possible to determine the oxygen pressure in the gas space of the cell; it amounted to 10^{-12}–10^{-14} atm. The impedance of the second platinum electrode (which was deposited on the surface of the solid electrolyte plate on the side opposite to that containing the drop) was neglected because of its large area. Separate experiments established that the auxiliary electrode was virtually unpolarised under the experimental conditions.

Fig. 2 presents curves characterising the dispersion of the resistance R and the capacitance C. The values of R and C were recalculated for a series-connected circuit. Evidently at a frequency of about 500 kHz a constant capacitance is reached and the measurements were made at this frequency. Having estimated the surface area of the junction between the metal drop at the electrolyte, the specific capacitance of the double layer was determined approximately. For silver and tin, it was found to be the same (20 μF cm^{-2}).

Somewhat later we made a detailed study at 970°C of the dispersion of the capacitance and resistance[6] using zirconium dioxide stabilised by yttrium oxide as the electrolyte. The oxygen pressure in the cell was maintained in the range 10^{-12}–10^{-14} atm, as before. The dispersion of the capacitance was investigated as a function of the yttrium oxide content in the solid electrolyte and the electrode potential. It was established that the capacitance in the series-connected circuit becomes constant at a frequency of 600 kHz. In the range of frequencies from 400 to 600 kHz the capacitance changed insignificantly—by up to 10%; therefore all subsequent experiments were performed at a frequency of 400 kHz, since the error in the measurement of the impedance components increased with a.c. frequency. This suggests that, with the series-connected resistance and capacitance, whose impedance is equal to that of the cell, the resistance refers to that of the electrolyte and the capacitance is that of the electrical double layer.

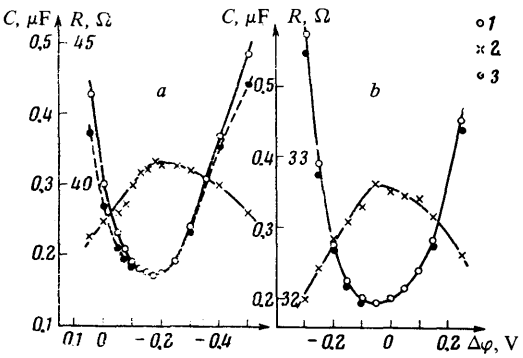

Figure 3. Variation of the differential electrical double layer capacitance (*1*) and of the resistance of the electrolyte (*2*) with polarisation for liquid silver and tin drops: *a*) tin; *b*) silver; points *3* represent the variation of the capacitance with allowance for the change in the area of the electrode/electrolyte junction as a result of the spreading of the drop.

We regarded the method described as satisfactory and used it to investigate the double layer capacitance on liquid silver and tin drops. The electrolyte disc had a diameter of 17 mm and was 1.8 mm thick; the diameter of the metallic drops was 0.7–1.0 mm. The decrease of the potential in the electrolyte may be neglected in view of the low polarising currents and the high conductivity of the electrolyte. Since the surface area of the platinum electrode was large, its contribution to the measured capacitance was neglected. The potential of the test electrode was reckoned relative to an air reference electrode.

Fig. 3 presents curves relating to the capacitance of the liquid silver and tin electrodes to polarisation. They have a deep minimum at specified potentials. The potentials of the minima on the capacitance curves for silver and tin are respectively −1.08 and −1.29 V. Curves relating the capacitance to the potential at different oxygen pressures in the gas phase were also obtained and it was found that a change in oxygen pressure does not affect the shape of the curves and the positions of the potential minima. One may conclude that the test electrodes are reversible with respect to oxygen. For this reason, regulation of the potential by altering the oxygen pressure in the gas phase or by polarisation with a direct current leads to the same result.

Fig. 3 also presents curves for the variation of the resistance of the electrolyte with electrode polarisation,

which has a distinct maximum. This can be explained by the fact that the surface tension at the boundary between the liquid drop and the solid electrolyte varies with polarisation, and hence the area of the junction between the drop and the electrolyte also varies. There is reason to believe that the resistance maximum corresponds to the interfacial tension maximum, i.e. to the zero-charge potential of the metal. Since the minimum on the capacitance curve and the maximum on the resistance curve occur at virtually the same potential, one may say that the potential of minimum capacitance coincides with the zero-charge potential. It might have been supposed that, owing to the variation of the area of the junction mentioned above, there is a change in the dependence of the capacitance on the potential and in the potential of minimum capacitance. However, the electrolyte resistances at different potentials show that this effect is very small and does not alter either the potential of minimum capacitance or the variation of the capacitance with potential (Fig. 3, dashed curve).

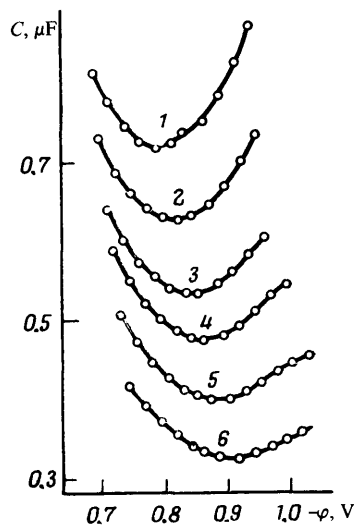

Figure 4. Variation of the electrical double layer capacitance with potential for a liquid silver electrode at different temperatures (°C): 1) 1123; 2) 1093; 3) 1060; 4) 1032; 5) 1001; 6) 969.

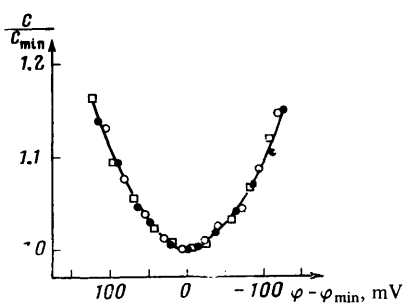

Figure 5. Variation of C/C_{min} with $\varphi - \varphi_{min}$ for three temperatures (1123°, 1060°, and 969°C); C is the electrical double layer capacitance at a potential φ and C_{min} and φ_{min} are the capacitance and potential corresponding to the minimum on the curve (see Fig. 4).

The temperature variation of the double layer capacitance was studied in the temperature range 970–720°C in an atmosphere of helium at a frequency of 400 kHz for a silver electrode in an electrolyte to which 8 mole % of yttrium oxide had been added[7]. The results (Fig. 4) show that the minimum capacitance increases with temperature and the minimum itself becomes somewhat sharper on the corresponding curves. However, when the capacitance is referred to its minimum value at a given temperature, then the points for all six temperatures fit on the same curve (Fig. 5). Hence one may conclude that the variation of the capacitance with potential is of the same type over the entire experimental temperature range. Indeed, if the shape of the curves were partly determined by the Faraday process, it would be difficult to expect such an agreement. Since the points on the $\lg C - 1/T$ curve fit satisfactorily on a straight line, one may conclude that the double layer capacitance increases exponentially with temperature over the entire experimental range of potentials. Similar capacitance–potential curves were obtained also in fused electrolytes[8].

III. ZERO-CHARGE POTENTIALS OF METALS

The capacitance–potential curves for dilute aqueous solutions also have a minimum coinciding with the zero-charge potential in the case of a symmetrical electrolyte. For aqueous solutions, a theory of this phenomenon was devised by Frumkin. However, there is as yet no corresponding theory for solid and fused electrolytes. Therefore further studies on the double layer capacitance at the boundary between liquid metals and a solid electrolyte are necessary, measurements of this kind in electrolytes with different defective structures and for a wider range of metals being particularly needed.

The zero-charge potentials of liquid silver, tin, gold, and copper were determined in the electrolyte 0.887 ZrO_2 + 0.08 Y_2O_3 + 0.04 Al_2O_3.[9] The solid electrolyte consisted of a disc 17 mm in diameter and 2–3 mm thick. The metal drop diameter was 2–3 mm. The electrolyte discs were prepared by the method already described. The measurements on silver and tin were made at 1085°C, on gold at 1190°, and on copper at 1174°C in an atmosphere of purified helium. The pressure of oxygen in helium was 10^{-12}–10^{-14} atm. The helium was freed from oxygen and the residual oxygen pressure was determined as in the measurements of the electrical double layer capacitance.

The zero-charge potential was determined by measuring the variation of the wetting angle θ with the potential. The wetting angle was determined from photographs of the drop profile, and $\cos\theta$ was plotted against φ. Under the conditions of a constant composition of the gas atmosphere, at the potential corresponding to zero charge the angle θ has the minimum value and the $\cos\theta - \varphi$ curves passed through a maximum. The platinum electrode, deposited on the lower side of the disc, was used to polarise the drop with a direct current. The test electrode potential was measured relative to an air reference electrode.

The curves obtained for silver and tin are presented in Fig. 6. Relative to the air reference electrode, the zero-charge potentials of silver and tin are respectively −0.97 and −1.23 V.[9] The high experimental temperature and the test metals were chosen so that the equilibrium oxygen pressure over the metal oxides was greater than the residual oxygen pressure in the cell at a given temperature. The following factor is striking. The difference between the zero-charge potentials of silver and tin

is $\varphi_0^{Ag} - \varphi_0^{Sn} = 0.26$ V. On the other hand, the difference between the potentials corresponding to the minimum double layer capacitances on the same metals is $\varphi_C^{Ag} - \varphi_C^{Sn} = 0.21$ V. These results show that the difference between the potentials of minimum capacitance for silver and tin is approximately the same as the difference between their zero-charge potentials. The agreement may be regarded as satisfactory bearing in mind that the accuracy of the determination of the zero-charge potentials is to within 25 mV.

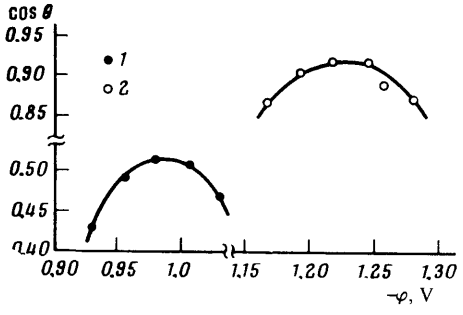

Figure 6. Variation of the cosine of the wetting angle with potential: 1) silver; 2) tin.

In a study of the correspondence between the potential of minimum double layer capacitance and the zero-charge potential in solid electrolytes[10] it was shown that such agreement can be accounted for when certain assumptions are made concerning the structure of the surface solid electrolyte. It is quite possible that such correspondence does not always obtain in solid and fused electrolytes.

The results of the measurements of the zero-charge potentials were adjusted to the same temperature (1085°C) by the procedure of Remez et al.[11] and are given in the Table.

The zero-charge potentials φ_0^M (M = metal).

Metal	Solid electrolyte		Aqueous electrolyte
	φ_0^M relative to air electrode, V	φ_0^M relative to φ_0^{Sn}, V	φ_0^M relative to φ_0^{Sn}, V
Silver	−0.97	+0.26	−0.32
Gold	−0.99	+0.24	+0.56
Copper	−0.85	+0.38	+0.47
Tin	−1.23	0.00	0.00

The values recommended by Leikis et al.[12] were used as the zero-charge potentials in aqueous solutions. The greatest difference relative to aqueous solutions is observed for silver. The zero-charge potentials of gold are of the same sign, but differ by 0.32 V. The difference for copper is a minimum (0.09 V). The experimental data obtained are insufficiently extensive to reach general conclusions on their basis. However, one may say a few words about the tabulated data.

Frumkin[1] demonstrated convincingly the role of the adsorption of not only ions but also neutral molecules both with and without intrinsic dipole moments. Furthermore, Frumkin[13] put forward the idea that, under certain conditions, the difference between the zero-charge potentials of two metals may be equal to the difference between their electrode work functions. Later Frumkin and coworkers[14] devised a detailed theory of this effect in which account is taken of the different degrees of adsorption of solvent molecules, particularly water molecules, on different metals. However, it is hardly useful to make such a comparison under the conditions of our experiments, since the electrode work functions of the metals investigated were determined at room temperature and our experimental temperature was in excess of 1000°C; it is necessary to determine the electrode work functions of the metals at high temperatures. Nor can one rule out the possibility that in our case adsorption, which may be different for different metals, plays a role in the zero-charge potential jump. For example, one may postulate the adsorption of oxygen ions or their vacancies.

The results of a study of the effect of carbon monoxide at the zero-charge potentials of silver and tin must be considered[15]. The experimental technique was as described above. When the gas phase contained 50 mole % of carbon monoxide, the zero-charge potential of silver was found to be −1.16 V relative to the air reference electrode. As stated above, in an atmosphere of helium this potential is −0.97 V. Thus the zero-charge potential of silver was displaced in the negative direction by 0.19 V as a result of the presence of carbon monoxide in the gas phase. The zero-charge potential of tin in the presence of 50 mole % of carbon monoxide was found to be −1.21 V, the corresponding value in helium being −1.23 V. The difference of 0.02 V is within the limits of the error of the measurements and one may assume that the change in the gas phase did not affect the position of the zero-charge point for tin.

The above shift of the zero-charge potential of silver can be tentatively explained by the adsorption of carbon monoxide molecules at the interface. Possibly chemisorption takes place in the present instance. The carbon monoxide molecule has a comparatively small dipole moment (0.12×10^{-18} absolute electrostatic units), but one cannot rule out the possibility that, as a result of adsorption, it acquires a larger dipole moment. It is appropriate to mention here our studies of the differential double layer capacitance on silver in an atmosphere of CO_2 and CO at 970°C.[16] The dependence of the capacitance on the potential was investigated and, as in an atmosphere of helium, curves with a deep minimum were obtained. The minimum capacitance increases with the CO content in the gas phase and the potential corresponding to the minimum on the curves also shifts in the negative direction.

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Electrochemical Methods of Studying Transfer Processes in Liquids

R.Sh.Nigmatullin, B.A.Kader, V.S.Krylov, and L.A.Sokolov

The theoretical basis of the electrochemical method of studying mass and momentum transfer in solid-liquid systems is outlined. Published work on the most important practical applications of the method is reviewed, including electrochemical modelling of heat and mass transfer processes, measurement of averaged and spectral hydrodynamic characteristics of the interaction between a flow of liquid and a solid surface, and the study of the fine structure of turbulent boundary layers. Theoretical and practical problems arising in electrochemical transducers are discussed. 135 references.

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I. INTRODUCTION

Modern scientific research relies increasingly on new instrumental means of obtaining information without using transducers liable to distort (to a greater or lesser extent) the phenomenon under study. Notable new techniques in the field of hydrodynamics and convective heat and mass transfer, which includes processes of outstanding importance in chemical and electrochemical technology, are laser anemometry, the radioactive indicator method, shadow photography, flow visualisation, etc. A special place among these methods belongs to the electrochemical method, in which an electric current is used as a measure of the rate of mass transfer from a flow of electrolyte solution to a conducting solid surface (the electrode).

The first attempts at electrochemical modelling of mass transfer processes in systems with a given configuration of hydrodynamic flows took place in the late 1940's and early 1950's [1,2]. More recently numerous groups of workers have demonstrated and examined in detail the possibilities of the method, and established its power in studies of transfer and exchange processes in liquid–solid and gas–liquid systems. The electrochemical method allows us to probe the structure of laminar and turbulent boundary layers (where the main resistance to heat and mass exchange resides), to obtain information on the fine structure of the turbulent flow in the viscous sub-layer of the boundary layer, to measure local values of the electrokinetic potential and of the rate of mass transfer, to investigate spatial and time correlations between local properties of hydrodynamic, concentration, and thermal fields, and to model the dynamic characteristics of many types of heterogeneous process of practical interest. As well as being very accurate and reproducible, electrochemical measurements are free from heat losses, they do not alter the area of the interfacial surface, and they are simple and convenient.

In recent years the electrochemical method of measuring viscous friction and of modelling heat and mass transfer processes in turbulent and in laminar flows has attracted the attention of researchers in many countries, including the USSR, USA, Germany, France, Japan, and others. The aim of this paper is to review the most important developments in the use of the electrochemical measurement method and of electrochemical modelling, to present the most interesting and useful results, and to discuss some problems in the theory of electrochemical transducers and some practical difficulties encountered in the application of this very valuable method of investigation.

II. PRINCIPLES OF THE MEASUREMENT OF THE RATE OF ELECTROCHEMICAL MASS TRANSFER UNDER STABILISED FLOW CONDITIONS

The electrochemical method of studying mass transfer relies on measuring the current density of an oxidation–reduction reaction at the surface of an electrode mounted in the wall of the vessel or exposed to the flow in some other way: under the chosen conditions the magnitude of the reaction current is determined by the hydrodynamic conditions of the process by which the reacting ions are supplied to the working electrode (concentration polarisation regime). In this case all the processes occurring at the working electrode (and therefore also the current flowing in the electrochemical cell consisting of a current source, anode, cathode, and flowing electrolyte) are described with sufficient precision by a system of hydrodynamic equations combined with the equations of convective mass transfer. The reaction rate is usually much greater than the rate of arrival of ions at the electrode surface by convective diffusion and migration, and therefore we can assume to a very good approximation that the concentration of reacting ions at the surface of the transducer is zero ($c_w = 0$). Hence the driving force of the ionic mass transfer ($c_0 - c_w$) is equal to the concentration of the ions at a point far removed from the electrode (c_0). Purely diffusional mass transfer is achieved by adding to the working solution an excess of an indifferent electrolyte which does not react electrochemically at the electrode

but minimises the contribution of electromigration to the transport of reacting ions. A typical current–voltage characteristic for a reaction showing concentration polarisation is reproduced in Fig. 1 together with a diagram of the circuit arrangement. In most cases the momentum associated with the substances taking part in the electrochemical reaction is small compared to the momentum of the solvent. Hence the properties of the hydrodynamic flow surrounding the electrode are practically unaffected by the electrochemical reaction.

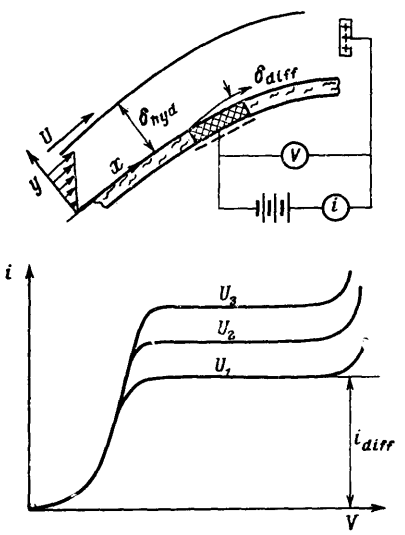

Figure 1. Schematic of the electrochemical measurement method and current–voltage characteristics for different flow rates of the solution ($U_1 < U_2 < U_3$): x is the spatial co-ordinate in the flow direction, y is the co-ordinate at right angles to the flow, δ_{hyd} is the effective thickness of the hydrodynamic boundary layer, δ_{diff} is the effective thickness of the diffusion boundary layer, i is the measured current, V is the voltage applied to the measuring cell, i_{diff} is the limiting diffusion current.

Often the size of the electrode in the flow direction (along the x axis) can be made much smaller than the characteristic hydrodynamic dimension, e.g. the cross-sectional diameter of a streamlined body or the distance from the electrode to the point of entry of the hydrodynamic flow. Hence, and with very few exceptions (for example, when very high pressure gradients are present in the system), the potential due to viscous fraction remains practically constant over the electrode surface. Constant tangential stress at the wall is a characteristic condition of systems consisting of a body immersed in a flow of liquid. A system of this type has been used[3] to study, by the electrochemical method, the detachment of a transverse flow surrounding a circular cylinder.

In any practical application of the electrochemical method it is important to bear in mind the following limitations, which apply to the chosen electrochemical reaction and electrolyte.

1. The reaction should not generate any products capable of disturbing the hydrodynamic conditions near the electrode.
2. The concentration polarisation at the measuring electrode should not be large enough to give rise to side reactions, which would alter the limiting diffusion current.
3. The reaction rate should be high enough to ensure that the effect of activation polarisation is negligible.
4. The reaction at the anode should be the inverse of the reaction at the cathode, to ensure that the concentration of the ions reacting at the working electrode remains constant during the experiment.
5. The composition of the electrolyte should be chosen so as to minimise the contribution of migration to the ionic mass transfer.
6. The electrolyte should be readily available in a pure form, adequately stable in solution, and it should offer a wide range of physical properties (viscosity, molecular diffusion coefficient, etc.).
7. The physical properties of the electrolyte (density, viscosity, diffusion coefficient, etc.) as well as their temperature and concentration dependence should be known with sufficient precision.
8. The electrolyte composition and the electrode reaction should be chosen so as to ensure reliable measurement of the limiting diffusion current in the concentration polarisation regime.

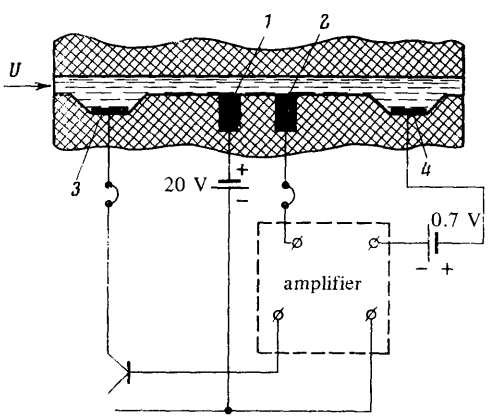

Figure 2. Electrochemical method employing two measuring electrodes: *1*) electrode for injecting electrically active material into the solution, *2*) electrode for monitoring the rate of transport of electrically active material by the flow, *3*) and *4*) auxiliary electrodes.

Two modifications of the electrochemical method have been described. The first relies on a single measuring electrode (transducer), which forms a reversible redox system with the electrolyte (see Fig. 1). The output signal of this transducer is the limiting diffusion current. Most of the published work on hydrodynamics and mass transfer was done by this method. However, the one-electrode transducer has a number of shortcomings, including excessive sensitivity of the calibration to the concentration of the species responsible for charge transfer at the interface, and also to the blocking of surface sites during the experiment.

The second modification of the electrochemical measuring system comprises two electrodes located at different points in the flow (Fig. 2). The first two-electrode flow-through cell (in the "disk and ring" configuration) was proposed by Frumkin and Nekrasov[4] for electro-analytical measurements. The electrically active products are generated by an electrochemical reaction in the central area of a rotating disk electrode, and detected by a peripheral, annular electrode mounted on the same disk. Many alternative forms of this system were subsequently developed for investigating the transport properties of liquids and gases and the special features of homogeneous and heterogeneous processes complicated by ionic mass transfer in solutions[5].

A cell consisting of a plane-parallel channel with two parallel strip electrodes separated by a narrow gap and mounted in one wall at right angles to the flow[6] offers a number of advantages over the "disk and ring" configuration. It is easier to construct, and it gives a theoretical description of the velocity and concentration profiles in a convenient analytic form. If the inter-electrode gap is small enough to allow the boundary diffusion layers to overlap, the measured current densities can give information on the hydrodynamic structure of the boundary layers under both the laminar and the turbulent flow regime. If the relationship between the measured limiting diffusion current and the parameters of the boundary layer velocity profiles is known in an analytic form we can determine the local hydrodynamic parameters of the flow with high precision (for example, the distribution of the average tangential stress at the wall, the spectral characteristics of the velocity and surface friction pulsations, etc.). Analytic solutions of the convective mass transfer problem, applicable in correlation measurements under laminar flow conditions, have been obtained for both the above forms of the two-electrode measuring cell[7-12].

III. CAPABILITIES AND ADVANTAGES OF THE ELECTROCHEMICAL METHOD

Electrochemical transducers are most effectively employed in modelling convective heat and mass transfer processes in liquids[1-12], and also in measurements of viscous flow stresses at the boundary between a turbulent liquid and a solid wall[13-18]. Electrochemical measurements are free from many of the difficulties associated with the methods traditionally used in experimental hydrodynamics, thermo-physics, and chemical technology. Thus even the first attempts at modelling mass exchange[1-3] were successful in demonstrating and exploiting the advantages of the electrochemical method. From a practical standpoint the most important of these advantages are the following.

1. Absence of thermal gradients, which introduce variations in the physical properties of the liquid across the thickness of the boundary layer.
2. The experimental analysis can be extended to the region of relatively high Prandtl numbers, where the temperature dependence of the properties of the liquid becomes most important.
3. In contrast to methods based on dissolution of the wall followed by measurement of weight loss, the electrode surface remains unchanged throughout the experiment.
4. Local measurements of the rate of mass transfer can be attempted because the electrode is only a few microns long in the direction of the flow.

Recent work on the measurement of boundary layer friction[19-23] has convincingly demonstrated the power of the electrochemical method and highlighted its advantages over the more traditional thermo-anemometric method. Firstly, electrochemical friction transducers are practically free from thermal losses, which are very difficult to estimate in thermo-anemometric transducers (especially the thin-film variety). Secondly, the liquid flowing round the solid body can be used as the working electrolyte in the electrochemical method, whereas the thermo-anemometric method requires a different, often very reactive, liquid. Thirdly, and this is very important, the diffusion coefficient of solutes is often several orders of magnitude smaller than the thermal diffusivity coefficient, and therefore (other conditions being equal) the information on the hydrodynamic flow reaches the electrochemical transducer from liquid layers closer to the solid surface than in the thermo-anemometric method. This is the reason why the electrochemical method was chosen to solve a number of fundamental problems concerning the fine structure of the viscous sub-layer. On of these problems was to establish in a functional form the law governing the change in the effective turbulent transport coefficients near a solid wall.

Some entirely new methods of studying boundary layer transport processes in gas–liquid flows have been developed[24] on the principle of electrochemical measurements. The problem of modelling tubular heat exchangers in chemical reactors has been largely resolved by an electrochemical study[25] of the interaction between the surface diffusion layers of closely spaced horizontal cylinders with their axes parallel and in the same vertical plane. The electrochemical method has been used with success also in measurements of large-scale velocity and pressure pulsations in the volume of a turbulent flow[26] and in the boundary layer detachment region[27].

IV. GENERAL THEORETICAL PROBLEMS

A large number of papers have been written on the theory of the electrochemical method of measuring rates of mass and momentum transfer[2,3,9-18,28-33]. Since the greatest theoretical and practical interest resides in the turbulent flow case we shall confine the discussion which follows to the present status of the theory of electrochemical transducers operated in the turbulent flow regime of the electrolyte solution.

1. Description of the Operation of Electrochemical Transducers in Terms of the Diffusional Boundary Layer Theory

The transducers best suited to the measurement of local characteristics of boundary layers have small dimensions in the direction of the mean flow. It becomes even more important to minimise the size of the transducer when we wish to measure the pulsation characteristics of the boundary layer, because in these measurements the sensitivity of the transducer decreases as its size increases (owing to the random changes in the magnitude of boundary layer friction along the transducer surface). An alternative explanation of the decrease in sensitivity with increase in size of the transducer is the averaging (over the transducer surface) of the current oscillations produced by various perturbations over distances smaller than the characteristic dimension (length) of the mass transfer region. For this reason the diffusion transducer is insensitive, in this region of geometrical dimensions,

to the fine structure of the spectrum of turbulent pulsations. We shall therefore discuss, in the first instance, only those transducers having sufficiently small dimensions in the direction of flow.

Consider an electrode of width h and length l, integral with the surface exposed to the flow, and located in the region of uniform tangential stresses. We shall impose the condition $l \ll h$, so that end effects at right angles to the flow direction can be ignored. This condition is satisfied, for example, by a ring electrode mounted flush with the tube wall in the region of hydrodynamically stabilised flow. We shall assume that the liquid flowing past the transducer contains a uniformly distributed passive additive at concentration c_0 (i.e. an additive which does not affect the flow dynamics). Let the origin of the spatial co-ordinates be at the front edge of the transducer, with the x axis along the direction of flow and the y axis at right angles to the planar wall. The stationary diffusion equation for planar turbulent two-dimensional flow, which applies in the regions where the passive additive is neither being generated nor consumed, can be written

$$\bar{u}_x \frac{\partial \bar{c}}{\partial x} = \frac{\partial}{\partial x}\left(D\frac{\partial \bar{c}}{\partial x} - \overline{u_x'c'}\right) + \frac{\partial}{\partial y}\left(D\frac{\partial \bar{c}}{\partial y} - \overline{u_y'c'}\right), \quad (1)$$

where the primes denote the pulsations of the instantaneous values with respect to their mean values. This equation can be solved by a number of procedures, the simplest of which (proposed by Boussinesq [34]) assumes a linear relation between the turbulent flows $\overline{u_x'c'}$, $\overline{u_y'c'}$ and the gradient of the mean concentration of additive. In the general case of an anisotropic velocity field Boussinesq's hypothesis can be formulated as

$$\overline{u_x'c'} = -K_{xx}\frac{\partial \bar{c}}{\partial x} - K_{xy}\frac{\partial \bar{c}}{\partial y}, \quad \overline{u_y'c'} = -K_{yx}\frac{\partial \bar{c}}{\partial x} - K_{yy}\frac{\partial \bar{c}}{\partial y}, \quad (2)$$

where the coefficients of the turbulent diffusion tensor (K_{ij}) are functions of the x and y co-ordinates. Most of the published theoretical work based on the hypothesis (2) assumes, often without justification, that the x and y axes are the main axes of the K_{ij} tensor, i.e. that $K_{xy} = K_{yx} = 0$. Other supplementary conditions have also been postulated, for example $K_{xx} = 0$ or $K_{xx} = K_{yy}$. Some workers assume diagonality of the K_{ij} tensor on the grounds that the directions of the x and y axes are defined by the same conditions as the hydrodynamically stabilised flow. None of these arguments is really strict [35]. We can only state that under stabilised flow conditions and near the walls, when the viscous flow stress τ_w does not vary in the direction of the flow, the components of the K_{ij} tensor are independent of the longitudinal co-ordinate x, i.e. that $K_{ij} = K_{ij}(y)$.

At very large values of the Prandtl diffusion number (the usual condition for mass transfer in liquid drops) the main resistance to mass transfer is concentrated in a thin boundary layer within which the velocity distribution can be assumed to be linear in the transverse co-ordinate y:

$$\bar{u}_x(y) = \frac{u_*^2}{\nu} y. \quad (3)$$

Here u_* is the characteristic turbulent pulsation velocity, related to the frictional stress τ_w at the wall by the expression $u_* = (\tau_w/\rho)^{1/2}$ where ρ is the density of the liquid and ν is the molecular kinematic viscosity. The components of the turbulent diffusion coefficient tensor in the boundary layer are given with sufficient precision by the first term of a Taylor series expansion in powers of y:

$$K_{ij} = \nu b_{ij}\left(\frac{yu_*}{\nu}\right)^{n_{ij}} = \nu b_{ij} y_+^{n_{ij}}.$$

An analysis of Eqn. (1) with the hypothesis (2) has shown [36] that at Prandtl numbers greatly in excess of unity the structure of the diffusion layer near the surface of the transducer is such that K_{yy} is the only components of the K_{ij} tensor making a significant contribution to the rate of mass transfer. Hence Eqn. (1) can be simplified, retaining only the component

$$K_{yy} = \nu b y_+^n, \quad (4)$$

where the exponent n is some effective value averaged over the thickness of the diffusion boundary layer, and in principle could be a function of the Prandtl number (note that for finite Prandtl numbers the expression of the K_{yy} coefficient in a Taylor series will contain, in general, more than one power of the dimensionless distance y_+). The experimental determination of the numerical value of the parameter n has been discussed several times in the literature [35-40], but there are still differences of opinion. The majority view is that the most probable range of n values is $3 \leqslant n \leqslant 4$. Thus an electrochemical investigation aiming to determine [41-45] "the limiting damping law of the turbulence" gave $n \simeq 3$. Other workers [46,47] find that $n \simeq 4$.

The general boundary conditions needed to ensure a unique solution of Eqn. (1) assume a constant concentration of the passive additive in the region far removed from the transducer surface

$$\bar{c}(x, \infty) = c_0; \quad \bar{c}(-\infty, y) = c_0$$

and they also assume a balance between the rate of the electrochemical reaction k and the mass flow of ions j_w to the surface of the planar diffusion transducer, determined by the rate of diffusion under conditions such that ionic migration under the influence of an electric field can be ignored:

$$D\frac{\partial \bar{c}}{\partial y}\Big|_w = \begin{cases} 0 & \text{for } x < 0 \text{ and } x > l; \\ kF(c_w) & \text{for } 0 \leqslant x \leqslant l. \end{cases}$$

The form of the function $F(c_w)$ is determined by the kinetics of the surface reaction. We shall assume in what follows that this reaction is of the first order, i.e. that $F(c_w) = c_w$, where the subscript w denotes conditions at the wall (i.e. for $y = 0$).

In the dimensionless variables of boundary layer theory

$$\vartheta = \frac{c_0 - \bar{c}}{c_0}, \quad X = \frac{x}{l}, \quad Y = \frac{y}{l}\left(\frac{u_*^2 l}{9Dvx}\right)^{1/3} = \frac{1}{\alpha}\frac{y}{l}$$

and introducing the above approximations Eqn. (1) becomes, for $\alpha \ll 1$,

$$(1 + \chi X^{n/3}Y^n)\frac{\partial^2\vartheta}{\partial Y^2} + 3Y^2\left(1 + \frac{\chi n}{3}X^{n/3}Y^{n-3}\right)\frac{\partial\vartheta}{\partial Y} - 9XY\frac{\partial\vartheta}{\partial X} = 0, \quad (5)$$

where $\chi = b\mathrm{Pr}^{(3-n)/n}(9lu_*/\nu)^{1/3}$ is the dimensionless parameter of the problem. The boundary conditions in dimensionless variables are

$$\vartheta(-\infty, Y) = 0; \quad \vartheta(X, \infty) = 0;$$
$$\frac{\partial\vartheta}{\partial Y}(X, 0) = \begin{cases} 0 & \text{for } X < 0 \text{ and } X > 1; \\ KX^{1/3}[\vartheta(X, 0) - 1] & \text{for } 0 \leqslant X \leqslant 1. \end{cases} \quad (6)$$

Here the symbol $K = k(9l\nu/u_*^2 D)^{1/3}$ denotes the dimensionless rate constant of the electrochemical reaction. If this constant is formally allowed to approach infinity the last of the boundary conditions (6) becomes

$$\vartheta(0 \leqslant X \leqslant 1, 0) = 1, \quad (7)$$

which corresponds to the limiting case of a fully polarised transducer. Kader and Dil'man [36] have obtained an analytic solution of Eqn. (5) for this case.

2. The Problem of Describing Small Transducers

Analysis of Eqn. (5) shows that the turbulent diffusion mechanism plays a negligibly small role if the longitudinal co-ordinate x is small enough. This conclusion has a simple physical significance: the pulsations of the hydrodynamic and of the concentration field are quickly damped near the wall, and have no effect on the rate of mass transfer at the wall itself (i.e. within the thickness of the diffusional boundary layer). It is important in practice to estimate the length of the electrode for which the contribution of turbulent mass transfer in the viscous layer can be ignored (allowing, however, for the real velocity profile, which can be quite different from the purely laminar profile). An exact solution of this problem for arbitrary values of n and b has been obtained[36]. The critical transducer length l_1, up to which the effect of turbulent transfer can be ignored, is given by the expression

$$l_1 = \left[\frac{3r_*(2n+3)\,\Gamma(1/3)\,\Gamma(2n/3)}{bn\,\Gamma^2(n/3)\,\Gamma\left(\frac{n+1}{3}\right)}\right]^{n/3} \frac{\nu}{9u_*}\,\mathrm{Pr}^{\frac{n-3}{3}}, \qquad (8)$$

where $\Gamma(x)$ is a gamma-function, and the quantity r_* denotes the precision (expressed as a percentage) of the experimental determination of the tangential stress at the wall.

Formula (8) becomes much simpler for $n = 3$, enabling the parameter b to be evaluated from experimental results (a value of approximately 10^{-3} was obtained by Kader and Dil'man[36]):

$$l_1 = 30\frac{\nu r_*}{u_*}. \qquad (8a)$$

In order to arrive at an estimate of the order of magnitude of the critical length l_1 under practical conditions we shall consider a transducer mounted in the wall of a tube of diameter $d = 1$ cm. Assuming that the transducer can measure the tangential stress with a precision $r_* = 10\%$, the critical length l_1 calculated by formula (8a) will vary with the Reynolds number Re for the flow in the tube (Re = Ud/ν, where U is the mean velocity of the flow) over the following range

$\mathrm{Re}\cdot 10^{-3}$	5	10	50	100	500	1000
l_1, cm	8.82	4.84	1.18	0.632	0.149	0.079

If the length of the electrode is less than l_1 there is a difficulty arising from the leading and the trailing edge of the transducer. In most of the papers quoted above the theory of diffusion transducers is developed in the boundary layer approximation, involving the assumption that the transducer is polarised over its entire length. It is well known, however, that the boundary layer approximation does not adequately describe the real distribution of the concentration near the edges of the transducer, i.e. in the regions of steeply changing wall conditions, where calculations based on this approximation can be seriously in error as a result of molecular diffusion in directions parallel to the wall. Thus the error becomes more significant with smaller transducers. Furthermore, since every point on the electrode surface is not equally accessible, and the reaction rate is finite, the concentration of reacting ions at the surface in the region of the leading edge must vary from its initial value to zero, i.e. some parts of the electrode are not polarised. Since the influence of the finite reaction rate is strong near both edges of the diffusion transducer, the two effects must be considered together.

However, all the work published so far deals with the two effects separately. Ling[48] has made a numerical analysis of the influence of edge effects in small, fully polarised transducers, while other workers[9,32] studied the concentration distribution along the surface of the transducer in the boundary layer approximation. The only fairly comprehensive numerical analysis of edge effects in systems designed for the measurement of stationary mass transfer and friction was published only recently[33]. On the other hand the effects are completely ignored in papers dealing with the sensitivity of electrochemical transducers to pulsations in the viscous sub-layer of the turbulent boundary layer[15,16,31,49].

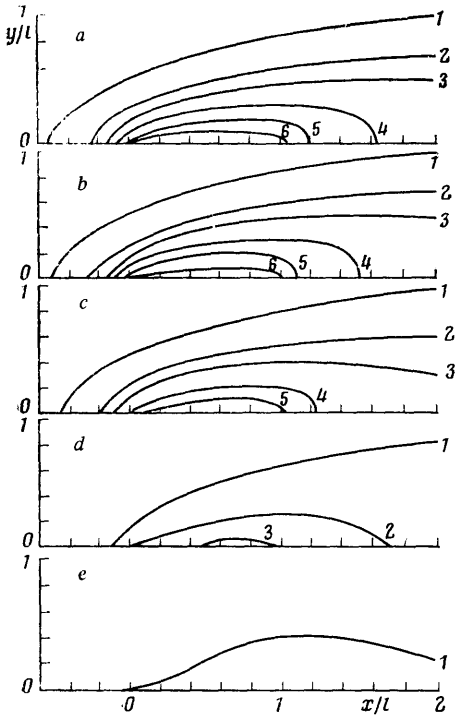

Figure 3. Concentration field above a thin-film diffusion transducer of dimensionless length $L = u_* l\sqrt{\mathrm{Pr}}/\nu = \sqrt{50}$ for different values of the dimensionless rate of electrochemical reaction K_0: *a*) $K_0 = \infty$, *b*) $K_0 = 10$, *c*) $K_0 = 1$, *d*) $K_0 = 0.1$, *e*) $K_0 = 0.01$; curves *1–6* correspond to θ values of 0.01, 0.1, 0.2, 0.4, 0.6, and 0.8 respectively.

Kader and Gukhman[33] solved the problem of mass transfer to the surface of an electrochemical transducer having a short length in the direction of the flow by using the average velocity profile of formula (3) and ignoring the influence of turbulent pulsations, but allowing for molecular diffusion in the longitudinal direction. Fig. 3, taken from that paper, shows the lines of equal concentration near the surface of diffusion transducers of equal length $l = (\nu/u_*)\,(50/\mathrm{Pr})^{1/2}$ for different values of the dimensionless complex parameter $K_0 = k\sqrt{\mathrm{Pr}}/u_*$ ($0.01 \leq K_0 < \infty$). The arbitrary edge of the diffusional boundary layer, corresponding to $\theta = 0.01$, is discussed in the same paper.

Longitudinal molecular diffusion results in a change in the concentration of reacting ions upstream from the

transducer. It is evident from the Figure that the diffusional boundary layer has a finite thickness at the leading edge of the electrode. However the influence of longitudinal molecular diffusion in this region becomes less marked as the parameter K_0 decreases. This effect stems from the peculiarities of the polarisation of thin-film diffusion transducers: the polarisation decreases as K_0 decreases, and for $K_0 = 0.01$ the arbitrary edge of the diffusional boundary layer ($\theta = 0.01$) coincides with the surface of the transducer. The surface concentration gradient is almost constant along the transducer under these conditions [33]. Calculation shows that even in small transducers operating under activation control the effect of longitudinal molecular diffusion is negligibly small.

An important characteristic of the efficiency of a thin-film diffusion transducer is the magnitude of the local diffusional flow at the leading edge ($x = 0$, $y = 0$). It can be shown [33] that this flow (j_{wf}) is given by the expression

$$j_{wf} = A\frac{u_* c_0}{\nu}\mathrm{Pr}^{-1/3}, \qquad (9)$$

where the coefficient A is finite for all values of the transducer length†, and depends on the value of K_0. Numerical values of the A coefficient for different characteristic values of K_0 are set out below:

K_0	0.01	0.1	1.0	10	∞
A	0.0099	0.091	0.575	1.65	2.40

3. Relative Role of Kinetic and Diffusion Effects for Transducers of Different Size

It follows from the above results that even for $K_0 = 10$ the transducer is not fully polarised ($\theta_w \neq 1$) over its entire length. The situation is illustrated in Fig. 4, which shows the distribution of the dimensionless surface concentration of diffusion transducers of different size ($5 \leq (u_* l\sqrt{\mathrm{Pr}}/\nu) \leq \sqrt{5000}$) for different reaction rates ($0.01 \leq K_0 < \infty$). It can be seen from the curves that the polarisation of the transducer increases with the length of the transducer and with K_0, in keeping with the expected decrease in the role of end effects with increase in the length of the transducer. The results of the analytic solution in the boundary layer approximation are also plotted in the Figure (broken lines). As expected, this solution gives a poor description of the real concentration field in the immediate vicinity of the leading and the trailing edge of the transducer, but it agrees very well with the numerical calculation over the central region. It follows from the general propositions of the boundary layer theory that the width of this region must increase with the dimensionless transducer length $L = u_* l\sqrt{\mathrm{Pr}}/\nu$. It is interesting to note that the direction of the difference between the analytic and the numerical solution (theoretical values of θ_w lower at the leading edge and higher at the trailing edge) suggests that the $\langle\theta_w\rangle$ values obtained by computer averaging over the length of the transducer for the boundary layer approximation should be fairly constant even for relatively short transducers. The present section is devoted to a discussion of these effects.

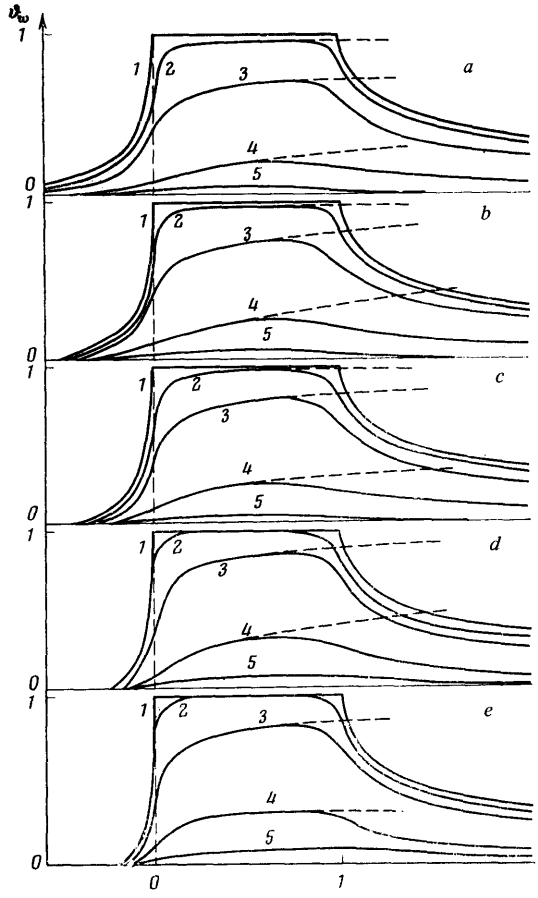

Figure 4. Concentration distribution on the surface of a thin-film diffusion transducer. The solid lines are given by the numerical solution, the broken lines by the analytic calculation in the boundary layer approximation: *a*) $L = 5$, *b*) $L = \sqrt{50}$, *c*) $L = 10$, *d*) $L = \sqrt{500}$, *e*) $L = \sqrt{5000}$; curves *1–5* correspond to values of the dimensionless rate K_0 of ∞, 10, 1, 0.1, and 0.01 respectively.

It follows from Eqn. (5) that the role of the edge effects may vary with L. Of course, for any value of L there will always be values of x so small that the product $\alpha^2\partial^2\theta/\partial x^2$ cannot be assumed to be small. Under these conditions the term $\partial^2\bar{c}/\partial x^2$ in Eqn. (1) cannot be ignored near the leading edge of the transducer, and the boundary layer approximation ($\partial^2\bar{c}/\partial x^2 = 0$) cannot be applied in this case. However, the fraction of the transducer surface for which this effect is appreciable decreases with increase of L.

†The conclusion from the exact solution of the diffusion problem (with allowance for longitudinal diffusion) that the diffusion flow is finite at the leading edge of the transducer is inconsistent with the results of later approximate calculations [134,135]. The contradiction probably arises from the assumption of a modified velocity profile in the latter work, corresponding to slipping of the liquid on the solid wall. However, even in the limit of a vanishingly small slip velocity the final analytic formula for the diffusional flow at the leading edge is incorrect, because at sufficiently small distances from the transducer surface the convective mass transfer due to slip dominates over the mass transfer associated with laminar flow in the viscous sub-layer.

Hence we may assume that for

$$\langle \alpha^2 \rangle = \int_0^1 \alpha^2(X)\,\mathrm{d}X = \left(\frac{9}{L^2}\right)^{2/3} \int_0^1 X^{2/3} dX \ll 1$$

the influence of edge effects on the general mass flow in a thin-film diffusion transducer is negligible. Thus we can say that in a transducer of length

$$l \gg l_2 = 12\,\frac{\sqrt{\nu D}}{u_*} \qquad (10)$$

the analysis based on the boundary layer approximation is quite correct. We note that the exact result obtained by Ling[48] for the case of $k \to \infty$ agrees fairly well with the estimate of Eqn. (10).

In a similar way we can estimate the length l_3 for which the rate of the electrochemical reaction plays a significant role. We use the last of the boundary conditions given in Eqn. (6). The electrochemical transducer can be said to be fully polarised when

$$\langle KX^{1/3} \rangle = \frac{k}{u_*}(9\,L\,\mathrm{Pr}^{2/3})^{1/3} \int_0^1 X^{1/3}\,\mathrm{d}X \gg 1,$$

i.e.

$$l_3 = 260\,\frac{u_*^2 D^2}{k^3 \nu}. \qquad (11)$$

The following interesting conclusions can be made from this estimate. As the frictional velocity increases, i.e. as the mean velocity of the flow passing the transducer increases, the length l_3 will vary if all other conditions remain the same. Depending on the value of the complex parameter K_0, this variation can be quite steep. If the constant k for the electrochemical reaction is small, even relatively long transducers may not be polarised over their entire length for typical working values of the overvoltage.

V. ELECTROCHEMICAL MODELLING OF MASS TRANSFER PROCESSES

Because of its many advantages, already mentioned, the electrochemical method has proved very successful in studies of mass transfer and phase exchange in solid–liquid systems. Initially the work was aimed at identifying improved solution compositions and the corresponding electrode reactions. It was usually carried out in measuring cells having well known hydrodynamic characteristics (rotating disk[50,51], rotating cylinder[52], flat plate[53], circular tube[54], and others). More latterly a very large number of publications on the electrochemical modelling of mass-transfer processes of practical interest has appeared in the literature (in particular, processes used in the chemical and petrochemicals industries). In many instances the experimental results have led to a broader and deeper physical understanding of the mass transfer mechanism, and have stimulated a great deal of theoretical work.

Both stationary and non-stationary methods have been used in electrochemical investigations of mass transfer. Since the two types of method have a number of individual features, we shall discuss them separately.

1. Stationary Methods

Electrochemical modelling has been used to study, with a precision unmatched by other methods, the mass recoil coefficients at the inlet of a circular tube as a function of length and of the Prandtl diffusion number[54–56]. By using thin annular electrodes these coefficients were measured at very small distances from the head of the mass transfer vessel (approximately one-thousandth of the radius of the tube). No previously known method could approach this level of precision.

Mass transfer in the gap between two rotating cylinders has been examined in detail[57–59]. The authors varied (over wide limits) the cell geometry and the rate of rotation of the cylinders, and they studied the influence of surface roughness on the rate of mass exchange between the phases. They were able to obtain quantitative empirical expressions describing not only the kinetics of stationary mass transfer, but also the conditions governing the hydrodynamic stability of the flow.

Interesting and unexpected results were obtained when electrochemical modelling was applied to rough surfaces. It was shown[60] that not only does the rate of mass transfer (relative to that in a smooth-walled system) not increase with flow velocity but it actually decreases, and may fall below unity[61]. These results, which were contrary to all expectations, were subsequently confirmed in more accurate experiments[45]. A theoretical explanation has recently been put forward, and generalised to a full quantitative theory of the phenomenon[62,63].

Very many electrochemical investigations using a rotating disk have been reported[42,64–72]. Some of them[64–67], confined to the purely laminar flow regime at the surface of the disk, were aimed primarily at measuring the diffusion coefficients of ions in electrolyte solutions. On the other hand, studies relying on turbulent mixing have dealt with the damping law of the turbulence in the immediate vicinity of the wall[42,68], with the influence of surface roughness on the rate of mass transfer[69,70], and with the local rates of mass transfer from small regions of various shapes on the surface of the disk[71,72].

Interesting results have been reported also on free convection near vertical and inclined plates with a smooth or a rough surface[73,74], near cylindrical objects under conditions when the curvature of the surface can influence the rate of mass transfer in the turbulent regime of free convection[75], and also on ionic mass transfer under free convection accompanied by heat transfer[76].

The stationary method has been used with success in system involving transverse flows over cylinders[3,77,78], in measurements of instantaneous local rates of mass transfer between an oscillating liquid film and a solid wall with a direct flow or a counter-flow of gas[79], and in studies of mass transfer in the turbulent flow beyond the point of greatest discontinuity in an annular tube[80]. Lastly, the stationary electrochemical method has been applied in studies of mass transfer in liquids have unusual properties[81].

2. Non-stationary Methods

It has been shown theoretically[82] that the stabilisation time of the concentration boundary layer formed at the surface of a flat plate with zero angle of attack by a sudden change in surface concentration is given approximately by

$$t_c \simeq \mathrm{Pr}^{1/3} x/U$$

and under normal conditions is measured in milliseconds. On the other hand the duration of the transient electrical process corresponds to the time constant t_{el} of the circuit

consisting of the double layer capacitance C_d and the ohmic resistance of the electrolyte R_{el} [83]:

$$t_{el} \simeq R_{el} C_d.$$

In most cases of practical interest the time t_{el} is of the order of a microsecond [84]. Hence we may assume that the diffusion-controlled reaction regime is established almost instantaneously. These considerations provide the basic concepts underlying the electrochemical modelling of non-stationary mass transfer processes: the non-stationary situation is modelled either by a sharp change in electrode potential or by a sharp change in hydrodynamic conditions.

The theoretical foundations of modelling non-stationary processes were laid by Lighthill [85], who studied the effect of small periodic perturbations in the main hydrodynamic flow on the surface friction and heat exchange coefficients at the liquid–solid interface. Others [86-89] developed theoretical analyses of heat and mass transfer processes from simple geometrical bodies (sphere and cylinder) oscillating in a liquid with an amplitude small in comparison with the characteristic dimensions of the system. The result of this work was a series of quantitative relationships defining the sensitivity of the electrode to mechanical oscillations in the measuring system. Mitchell and Hanratty [15] carried out numerical calculations of non-stationary models of mass and momentum transfer processes near walls exposed to turbulent flows, and obtained a solution of the convective diffusion equation at the wall of an annular tube in the presence of periodic perturbations of the pressure gradient. A theoretical discussion [90,91] of the convective diffusion of a passive additive in an arbitrary velocity field opens the possibility of measuring large-scale velocity pulsations by a correlation method. Lopatin and coworkers [92] have looked for an analytic form of the function describing the response of the surface of a rotating disk electrode to periodic perturbations of the concentration of reacting ions in the bulk of the solution.

Among the experimental studies of non-stationary mass transfer we should mention, first of all, a systematic investigation of the development of a diffusion boundary layer at a metal plate exposed to a stationary flow of electrolyte solution at different angles of attack [93-95], and also some work on mass transfer to a transversely located cylinder [96,97] and to the wall of an annular tube [98]. Mass transfer in non-stationary flows was studied experimentally near the surface of a vibrating disk [99], and also in the case of pulsating flow in a tube [100,101]. Much of this work was stimulated by the needs of a new and rapidly expanding branch of technology: chemotronic instrumentation, i.e. the construction of apparatus for the translation of non-electrical quantities into electrochemical signals [102-105]. Another important application of non-stationary methods is in the development of electro-diffusion anemometers, whose operating principle has been discussed in detail [28-32,49].

VI. ELECTROCHEMICAL METHODS OF STUDYING HYDRODYNAMIC PROBLEMS

Accurate methods of determining experimentally the hydrodynamic structure of various flow configurations (mean velocity and tangential stress profiles, fluctuation parameters associated with turbulence, etc.) are needed to provide objective information on the mechanism of turbulent transfer near a solid surface, and thus to test the many hypotheses to be found in the literature on the fine structure of boundary layers. They are also needed for reliable engineering calculations of the hydraulic parameters of turbulent flows in industrial mass exchange apparatus, chemical reactors, thermophysical plant, and other systems.

As pointed out above, the electrochemical method offers very attractive possibilities in all these areas. Its ability to measure with great precision both the averaged and the spectral characteristics of flow near the walls of channels and of submerged bodies has been repeatedly demonstrated. With gas–liquid flows within channels the electrochemical principle offers the only possibility of measuring the true tangential stress at the wall [32,106]: all other known methods (such as the pressure drop method, the floating element method, the Stanton tube methods, etc.) are either totally inapplicable or insufficiently accurate. Electro-diffusion transducers have been used for direct measurements of surface friction and its pulsations for different flow regimes of two-phase media in vertical and horizontal tubes, for accurately establishing "regime charts" of the parameters governing the various flow regimes of two-phase mixtures, and in studies of the hydrodynamic analogy between bubbling and ebullition under forced flow conditions [24,32].

The spherical electrochemical transducer [107,108] has been found very effective for the measurement of velocity profiles in laminar flows. It consists of a spherical platinum electrode 0.5 to 1.0 mm in diameter, located in the flow region of interest and operated under conditions of concentration polarisation. Concentration and temperature errors are avoided by inserting into the flow an auxiliary micro-electrode whose output is independent of the flow rate and is determined by the concentration of the depolariser (oxygen) and by temperature. This transducer can measure local flow rates with a spatial resolution limited by the width of the disturbed hydrodynamic region. For $Re < 1$ this region extends over approximately six electrode radii on either side of the transducer. At higher Reynolds numbers the width of the disturbed region decreases.

Significant advances have been made in the design and practical application of electrochemical surface friction transducers. Some theoretical aspects of the operation of these transducers are discussed in detail in the following sections.

1. Measurement of Mean Tangential Stresses

For a fully polarised transducer operating under laminar diffusion layer conditions (when the ionic mass transfer is unaffected by turbulent pulsations in velocity and pressure) Eqn. (5) with the boundary conditions (6) takes the form of the well-known Leveque problem [109]

$$\frac{d^2\vartheta}{dY^2} + 3Y^2 \frac{d\vartheta}{dY} = 0; \quad \vartheta(\infty) = 0; \quad \vartheta(0) = 1. \tag{12}$$

The solution of this problem, in the form

$$\vartheta(Y) = 1 - \frac{3}{\Gamma(1/3)} \int_0^Y \exp(-x^3)\, dx, \tag{13}$$

allows us to establish the relationship between the ionic mass flow j_w to the electrode, proportional to the electric current in the measuring cell, and the tangential stress τ_w at the wall:

$$j_w = 0.807\, c_0 \left(\frac{D^2 \tau_w}{\rho \nu l}\right)^{1/3}. \tag{14}$$

We should remember that the length l of the transducer must be less than the quantity l_1 defined by Eqn. (8). (This equation imposes a limit on the range of dimensions for which the contribution of the turbulent mass transfer mechanism can be ignored.) At the same time, the length of the transducer should be large enough to justify neglecting edge effects, with the assumption that the transducer surface is fully polarised. According to the estimates made above, the condition is $l \geqslant \max(l_2, l_3)$, where l_2 and l_3 are the characteristic lengths defined by Eqns. (10) and (11).

The experimental conditions for the measurement of the mean wall friction, and the constructional details of the measuring cells, have been discussed by several workers [13-15,30,110-115]. These papers describe measurements of the tangential stress at the wall of a cylindrical tube, of a plane-parallel channel, and of a two-dimensional cavity in liquid and gas–liquid flows, and they deal with the interaction between a liquid (laminar, or turbulent) and a solid wall under thin-layer flow conditions. The electrochemical method has been used to study in detail the stabilisation of local friction in the initial portion of a plane-parallel channel [116], in flows under a longitudinal pressure gradient [117], and in flows involving complex vortex structures [30].

The correlation method of measuring the averaged characteristics of turbulent flows in boundary layers [30] has great conceptual and practical interest. One variant of this method involves monitoring the correlation between the random pulsations of the flows on two planar electrodes mounted on the experimental plate, mutually parallel and with their edges at right angles to the flow direction. The measured correlation function R is related to the pulsations of the currents at the two electrodes (i_1 and i_2) by the expression

$$R(|x_1 - x_2|, \tau) = \frac{1}{T}\int_0^T i_1(x_1, t)\, i_2(x_2, t - \tau)\, \mathrm{d}t, \qquad (15)$$

where τ is the variable time-lag of the current i_2 with respect to i_1, T is the measurement time ($T \gg \tau$), and x_1 and x_2 are the co-ordinates of the electrodes (the linear dimensions of the electrodes are assumed small in comparison with the distance $l = x_1 - x_2$). The function R goes through a maximum at $\tau = \tau_m$, given by $\tau_m = l/V$ where V is the mean velocity of the turbulent vortices in the disturbed region of the diffusion boundary layers at the electrodes. In this way we can measure the characteristic velocity V of the turbulent vortices near the wall by noting the time τ_m.

The correlation method can be used also to measure the tangential stresses in a laminar flow by introducing concentration markers from a third, auxiliary electrode a short distance in front of the first electrode.

The most characteristic feature of the correlation method is the lack of dependence of the measurement error on the diffuseness of the concentration wave in the region of the two electrodes, and on the presence of obstructions.

2. Measurement of the Spectral Characteristics of Wall Friction

The turbulent pulsations of the surface friction can be quantitatively characterised by the mean-square fluctuation of the friction $\overline{(\Delta\tau_w)^2}$, which is related to the distribution function of the spectral density $\epsilon_\tau(\omega)$ by the expression [118]

$$\overline{(\Delta\tau_w)^2} = \int_0^\infty \varepsilon_\tau(\omega)\, \mathrm{d}\omega, \qquad (16)$$

where the integration is carried out over the whole range of pulsation frequencies ω. The spectral density function describing the pulsations of electric current $\epsilon_i(\omega)$ can be determined by analogy with the function $\epsilon_\tau(\omega)$. The functions $\epsilon_\tau(\omega)$ and $\epsilon_i(\omega)$ are interrelated by the expression

$$\varepsilon_i(\omega) = |\xi(i\omega)|^2 \varepsilon_\tau(\omega), \qquad (17)$$

where $\xi(i\omega)$ is termed the response function of the diffusion layer to harmonic pulsations of the velocity of the liquid with frequency ω (the symbol i denoting an imaginary quantity). If the time-average frictional stress at the wall is termed $\overline{\tau_w}$, we can obtain the following relationship between the mean square frictional stress fluctuation $\overline{(\Delta\tau_w)^2}$ and the mean square total current $\overline{(\Delta I)^2}$ by using expressions (16) and (17):

$$\frac{\sqrt{\overline{(\Delta\tau_w)^2}}}{\overline{\tau_w}} = \frac{\sqrt{\overline{(\Delta I)^2}}}{\overline{I}} \left(\int_0^\infty \frac{\varepsilon_i(\omega)\, \mathrm{d}\omega}{|\xi(i\omega)|^2}\right)^{1/2}, \qquad (18)$$

where $\overline{I}$ is the time-average current. In the case of a rectangular electrode of area S and length l the mean current can be expressed in terms of the mass flow of ions, given by formula (14), by introducing the simple relationship $\overline{I} = mFSj_w$ where m is the number of electrons transferred across the metal–solution interface by the elementary electrochemical reaction and F is the Faraday.

It follows from Eqns. (17) and (18) that the spectral and the averaged characteristics of the pulsation field of the tangential stresses can be determined simply from a knowledge of the response function of the diffusion layer $\xi(i\omega)$. The latter can be evaluated, in principle, by solving the equation for a non-stationary boundary diffusion layer with a velocity profile given by the first non-vanishing term of the expansion in powers of the distance from the wall:

$$u_x = \frac{\overline{\tau_w} y}{\rho\nu}(1 + \lambda f(t)), \quad u_y = 0, \qquad (19)$$

where $f(t)$ is a harmonic function of time and λ is the dimensionless amplitude of the pulsating velocity field.

An analysis of the solution of the non-stationary convective diffusion equation in the velocity field given by formula (19) with $f(t) = \exp(i\omega t)$ has shown [85] that the response function $\xi(i\omega)$ can be expressed as follows to a second-order approximation in the terms of the dimensionless amplitude λ:

$$\xi(i\omega) = 1 + \lambda\xi_{1,1}e^{i\omega t} + \frac{\lambda^2}{2}(\xi_{2,0} + \xi_{2,2}e^{2i\omega t}) + 0(\lambda^3), \qquad (20)$$

where $\xi_{1,1}$, $\xi_{2,0}$, and $\xi_{2,2}$ are functions of the longitudinal co-ordinate x.

Several workers [15,30,119,120] have tried to calculate the functions $\xi_{1,1}$, $\xi_{2,0}$, and $\xi_{2,2}$ by introducing various simplifying assumptions. Analytic expressions were obtained for the function $\xi_{1,1}(x)$ with small or large values of the parameter $\epsilon = (\rho\nu l\,\omega^{3/2}/\tau_w D^{1/2})^{2/3}$. In physical terms, this parameter denotes the ratio of the squares of the thickness of the stationary diffusion boundary layer (in the absence of velocity pulsations) and the periodic diffusion boundary layer [30,120]. The contribution from second-order amplitude terms has also been estimated, and it was shown that both high-frequency and low-frequency pulsations can lower the time-averaged and the area-averaged mass transfer coefficient [119,120].

Methods of determining experimentally the pulsation characteristics of the turbulent velocity field in boundary layers close to the wall have been developed from the published analytic expressions for the response function [30].

An experimentally simple but effective method of measuring surface friction is based on non-stationary pulse measurements [121]. The method does not differ in principle from the method shown in Fig. 2. A pulse of electrically active material is injected into the hydrodynamic flow by an electrochemical reaction at the upstream "marker" electrode *1* (see Fig. 2). This pulse is carried by the flow to the measuring electrode *2* (arbitrarily called the "counting" or indicator electrode). A definite time elapses between the application of the pulse at the marker electrode and its arrival at the counting electrode. This time (called the time-lag t_l) depends on the hydrodynamic regime and can be used as a measure of its intensity.

The time-lag can be evaluated from the following considerations. The total transfer time includes a term for the diffusion of the electrically active material to some distance y at right angles to the flow, and a term for the hydrodynamic transport to the indicator electrode. The diffusion time includes diffusion from the marker electrode and diffusion to the counting electrode. To the accuracy of the numerical factor of the diffusion time we can write

$$t_{diff} \simeq \frac{y^2}{D}. \tag{21}$$

The hydrodynamic time is given by the expression

$$t_{hyd} \simeq \frac{\rho \nu x}{\tau_w y}, \tag{22}$$

where x is the distance between the marker and the counting electrode. Thus the total transfer time is

$$t_{tot} \simeq \frac{y^2}{D} + \frac{\rho \nu x}{\tau_w y}. \tag{23}$$

It follows from Eqn. (23) that we can define a distance y_{min} corresponding to the minimum transfer time. Evidently, the smallest transfer time is equal to the time-lag. Hence we conclude that the thickness of the diffusion layer within which the electrically active material is transported from one electrode to the other is given (to the nearest order of magnitude) by the expression

$$y_{min} \simeq \left(\frac{\rho \nu x D}{\tau_w}\right)^{1/3}, \tag{24}$$

i.e. it is equal to the thickness of the stationary diffusion layer. Hence the time-lag is of the same order of magnitude as the relaxation time of the diffusion layer:

$$t_l \simeq \left(\frac{\rho \nu x}{D^{1/2}\tau_w}\right)^{2/3}. \tag{25}$$

It follows that the time-lag is inversely proportional to the tangential frictional stress to the power 2/3. This analysis (which ignores the finite size of the electrodes themselves) provides a numerical value of the multiplier needed in Eqn. (25): a recent calculation [120] gives

$$t_l = 2\left(\frac{\rho \nu x}{D^{1/2}\tau_w}\right)^{2/3}. \tag{26}$$

The frequency method [121] is closely related to the pulse-time method. If the electrodes *1* and *2* are included in the negative feedback circuit of an amplifier, undamped oscillations will occur at some frequency. The oscillation condition is a phase shift of 180° between the signals at the marker and the counting electrode. Using Eqn. (26), the frequency of the resulting oscillations can be expressed as

$$f = \frac{1}{2t_l} = \frac{1}{4}\left(\frac{D^{1/2}\tau_w}{\rho \nu x}\right)^{2/3}. \tag{27}$$

Thus the frequency of the oscillations is directly proportional to the tangential stress arising from viscous friction to the power 2/3.

The analysis applies also to a turbulent boundary layer if the diffusional transport in the normal direction takes place within the thickness of the laminar diffusion layer. Since the thickness of the diffusion layer increases only as far as the edge of the indicator electrode, the permissible size x of the electrode system [see formula (8)] should include the length of the marker electrode and the length of the inter-electrode gap. The length of the indicator electrode should have only a second-order effect on the sensitivity of the electrochemical measuring system.

Since the frequency of the electrical oscillations is linearly related to the tangential frictional stress to the power 2/3, the sensitivity η of the electrochemical transducer can be conveniently defined as

$$\eta_{2/3} = f\bar{\tau}_w^{-2/3} = \frac{D^{1/3}}{4}(\rho \nu x)^{-2/3}, \tag{28}$$

where the subscript 2/3 indicates non-linearity of the transformation.

A very interesting situation arises for large values of the tangential stress, when the thickness of the turbulent diffusion layer becomes less than the thickness of the laminar diffusion layer. Whereas in the case of a laminar diffusion layer the time-lag of the pulse includes the diffusion time of the electrically active material in the normal direction and the time for hydrodynamic transport in the tangential direction, under the conditions of a turbulent diffusion layer the only slow transfer step is the transport through the turbulent diffusion layer. The electrically active material which has passed through the turbulent diffusion layer is rapidly carried through the required distance in the tangential direction. Leaving aside the problem of the sensitivity which the indicator electrode must have in order to detect the concentration pulse, we can state that undamped oscillations will be generated in a turbulent diffusion layer and that their frequency will be of the same order as the relaxation frequency of the turbulent diffusion layer.

Assuming an effective exponent (n) of 4 for the damping law of the turbulent pulsations near the solid wall, given by Eqn. (4), we can apply the expression $f \simeq D\delta_{hyd}^{-2}$ and estimate the frequency of the resulting oscillations as

$$f \simeq \frac{\bar{\tau}_w}{\rho \nu} \mathrm{Pr}^{-1/2}. \tag{29}$$

The frequency of the oscillations for a predominantly turbulent diffusion layer is proportional to the first power of the tangential frictional stress and is independent of the inter-electrode distance over a wide range.

According to Eqn. (29) we can conveniently define the sensitivity of the transducer as

$$\eta_1 = f/\bar{\tau}_w = D^{1/2}/\rho \nu^{1/2}, \tag{30}$$

The subscript 1 denotes linearity of the transformation.

The electrochemical frequency method of measuring friction was tested experimentally using a model of the electrochemical tangential stress transducer [121] made of electrically insulating material. The electrode system was mounted flush with the surface exposed to the liquid flow, and consisted of three parallel linear electrodes made of platinum and oriented at right angles to the flow direction. The electrodes were connected in the following sequence along the flow: marker electrode, counting electrode, and common electrode. Sea-water was used as the electrolyte. The application of a positive potential to the

marker electrode induced an electrochemical reaction at the electrode surface, causing oxidation of chloride ions to chlorine atoms. The counting electrode was connected to a constant negative polarity of sufficient magnitude to draw the limiting current of the chlorine–chloride redox system. The amplifier input was connected to the counting circuit, and the output to the marker circuit. Self-oscillations were produced at some definite ratios of the current in the marker circuit and in the counting circuit. The phase-shift angle between the marker current and the counting current, and hence the self-oscillation frequency, is a function of the tangential frictional stress.

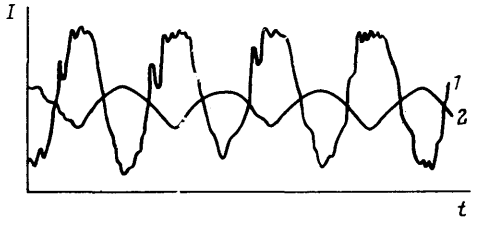

Figure 5. Oscillographic determination of the frequency of the electrical signals generated in experiments on the electrochemical measurement of tangential stress: *1*) marker current , *2*) counting current.

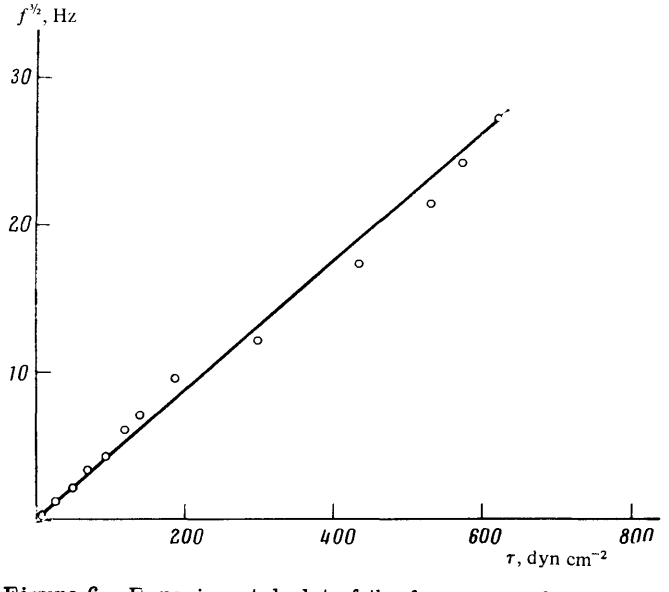

Figure 6. Experimental plot of the frequency of generated oscillations against the tangential stress at the solid wall ($f^{3/2}$ against τ).

The experimental results are summarised in Figs. 5 and 6. The generation frequency was measured oscillographically (a typical trace is shown in Fig. 5). Fig. 6 shows an experimental plot of the generation frequency against the tangential frictional stress for a laminar flow regime. It can be seen that the power law of the experimental plot is close to the theoretical value.

Electrochemical transducers for the measurement of local velocity distributions in a flow have been widely used in recent years. These devices (wedge-shaped, spherical, or circular) are positioned in the flow of electrolyte at right angles to the flow, and they do not differ in principle from the wall-mounted electrodes described above.

VII. STUDY OF THE STRUCTURE OF TURBULENT FLOW

The electrochemical method can be used to investigate the mechanism of momentum and mass transfer in liquid layers a few tens of microns thick. Hence it offers a unique and most effective means of probing the fine structure of the turbulence in the viscous sub-layer of a turbulent boundary layer. We have already referred to the work[41-44] on the limiting damping law of the turbulence at a solid wall. The structure of the turbulence has been investigated also by other workers[13-18,38,122-124], who studied vortex configurations, the rate of propagation of vortices by convection in the flow, and the microscopic and macroscopic features of turbulence.

Improved modifications of the electrochemical method are currently being developed for studying the structure of hydrodynamic flows and for measuring average and local rates of mass transfer[125]. One of these modifications relies on electrochemiluminescence, whose intensity is proportional to the local rate of mass transfer. Interesting results can be obtained by exploiting the colour change of some electrolytes under the influence of local changes of pH. A procedure for visually observing and studying velocity fields is based on this phenomenon.

VIII. SOME PRACTICAL PROBLEMS

In our opinion, the most important scientific and engineering problems still to be solved in order to ensure wider practical exploitation of electrochemical modelling are the following: 1) the choice of electrochemical systems with the required physical and transport properties; 2) the theoretical understanding and practical control of blocking effects at the transducer surface during operation, and of transducer activation; 3) a more detailed study of correlation and other measurements using transducers of very small dimensions (in particular, for the measurement of transverse velocity pulsations); 4) an appreciation of the role of turbulence on the response of physically large transducers. Some of these problems have been discussed repeatedly in the literature, and have been the object of special investigations. For example, Eisenberg and coworkers[52] have discussed the choice of the best electrolytes and electrode reactions for modelling mass transfer. No less important is the problem of transducer blocking, which we shall briefly review in the following paragraphs.

A common problem in electrochemical measurements extending over long periods of time is the possible contamination of the electrode surface (e.g. by adsorbed surface-active materials, insoluble products of the electrode reaction, oxide films, evolved gas bubbles, etc.). These contaminants can inhibit the access of the reacting species to the transducer surface, and thus lower the rate constant of the electrochemical indicator reaction. The parasitic resistance experienced by the ionic mass transport as a result of the presence of contaminating surface layers adds

to the difficulty of interpreting the electrochemical mass transport data and introduces a need for empirical correction factors. Partial surface blocking is the most likely explanation of the substantial differences (20–30%) between measurements of stabilised electrochemical mass transfer obtained by different methods under identical hydrodynamic conditions (see, for example, Refs. 54 and 55).

Since it is impossible in practice to achieve complete control over the surface conditions of the transducer, especially in large-scale apparatus containing large volumes of electrolyte, we must continue to search for theoretical methods of assessing (within the limits imposed by the unavoidable assumptions) the effect of surface blocking on the results of electrochemical measurements.

The methods used to describe convective heat and mass transfer processes in systems with non-uniform surface activity are highly relevant to our problem. One of the simplest yet fairly typical models of a heterogeneous surface consists of a rotating disk with one or more annular active regions isolated from the other regions by the disk[126,127]. Another typical model consists of a flat plate with alternating active and "lacquered" parallel bands at right angles to the direction of the flow[6,128]. The effect of surface contamination on the efficiency of electrochemical diffusion transducers can also be described in terms of a model assuming a continuous variation in activity along the phase boundary[33,129-131]. Kader and Gukhman[33] allowed for partial blocking of the transducer surface by assuming a thin, uniform layer offering a constant resistance to the ionic mass transfer. The mass flow of reacting ions through this layer was assumed proportional to the difference in concentration of the ions on the two sides of the layer. In this way the blocking effect could be allowed for by replacing (in the boundary condition) the true rate of the electrochemical reaction by some arbitrary quantity linearly related to the surface concentration of reactant.

The parameters of the model can often be optimised by comparing the results of model calculations with experimental data. However it is far preferable (though not always possible in practice) to seek information on the distribution of the blocking impurities on the electrode surface. If this information can be obtained the apparent rate of the electrochemical mass transfer process can be calculated, in principle, either analytically or by numerical methods. Approximate methods of calculating the rate of mass transport to isolated active regions of arbitrary shape on the surface of a rotating disk have very recently been proposed, assuming a laminar flow regime[132,133].

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We have attempted a general review of the theoretical foundations, practical applications, prospects, and outstanding problems of the electrochemical method of studying and modelling transport processes in liquids. The method is relatively new, but its effectiveness and generality have already been amply demonstrated in practice. The large effort currently being devoted by various research teams to further developments and improvements of the electrochemical method justifies the belief that many fundamental problems in the theory and practice of mass transfer and inter-phase exchange will be solved with the help of this method.

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The Influence of the Nature of the Metallic Phase on the Structure of the Electrical Double Layer and the Kinetics of the Evolution of Hydrogen

U.Palm and V.Past

The influence of the crystallographic structure of the surface of a solid electrode and of the specific interaction between the solvent and the metal on the properties of the electrical double layer and the adsorption of ions and dipolar molecules on metals which do not adsorb hydrogen is examined. The problem of the influence of the structure of the electrical double layer on the kinetics of the evolution of hydrogen on bismuth, tin, lead, and cadmium, in acid and alkaline solutions is discussed.
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I. INTRODUCTION

Significant progress has been achieved in the last decade in quantitative studies of the structure of the electrical double layer, adsorption phenomena, and the laws governing the occurrence of electrochemical reactions on electrodes made of a wide variety of different metals. Metals on which conditions of ideal polarisability can be achieved to a satisfactory degree of approximation over a wide range of potentials φ are the most suitable for a quantitative test of the theoretical concepts concerning the structure of the electrode/solution interface[1-4]. In contrast to mercury, on solid electrodes a fundamentally new problem involves the study of the influence of the crystallographic characteristics of the surface of the metal on the structure of the electrical double layer, particularly its dense component (together with the problem of the influence of the chemical nature of the metal). The investigation of the structure of the interface on different faces of a single crystal is most promising in this sense.

Frumkin and coworkers[5,6] showed that one of the most exact methods for the study of the structure of the electrical double layer involves the measurement of the variation of the differential capacitance C with φ. However, in the measurement of the capacitance of solid metals it is necessary to eliminate the sources of the false frequency dispersion of the capacitance (roughness of the surface, the phenomenon of saturation, etc.)[3,4,7,8]. A number of methods for smoothing the surfaces of test electrodes have now been developed and successfully applied.

Frumkin and coworkers[9] showed that surface fusion of the metal constitutes a promising method for the preparation of solid electrodes with the roughness coefficient of the surface close to unity. A special procedure for the preparation of drop-shaped surface-fused electrodes with a smooth surface has been developed in the Electrochemical Laboratory at the Tartu State University[10,11]. Subsequently the procedure was used to prepare drop-shaped antimony[12], tin[13], and cadmium[14] electrodes. Fig. 1 shows that the variation of $1/C$ with the reciprocal of the diffuse layer capacitance $1/C_d$ of bismuth can be represented over a wide range of KF concentrations (0.001–2 M) and for different surface charges ϵ by straight lines with an average reciprocal of the slope of 1.01–1.02.[15] It has been shown[16] that the slope of the linear plot of $1/C$ against $1/C_d$ for $\epsilon = 0$ differs from unity by less than 10% in the case of antimony. These results show that surface-fused electrodes have a perfectly smooth surface.

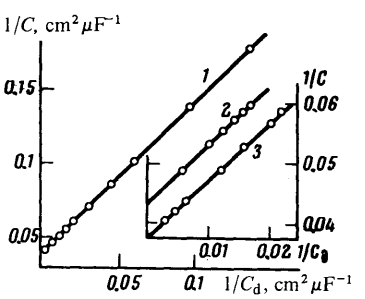

Figure 1. Variation of the reciprocal of the differential capacitance $1/C$ with the reciprocal of the capacitance of the diffuse layer $1/C_d$ in the range of KF concentrations from 0.001 to 2.0 M for different values of ϵ (C cm^{-2}): 1) 0; 2) −3; 3) +2.

Among solid electrodes, bismuth is the metal which exhibits the widest (after mercury) range of ideal polarisability potentials in both aqueous[10,15] and non-aqueous[17-19] media. On the other hand, many of the physical and chemical properties of bismuth differ significantly from those of mercury and metals resembling it, and lead to its classification as a semimetal. Bismuth is therefore an

interesting object of study for the elucidation of the influence of the nature of the metallic phase and also of the crystallographic structure of the surface on the double layer parameters and adsorption. In this review attention is concentrated on the following problems in relation to bismuth together with the relevant data for other electrodes:

(1) the influence of the crystallographic structure of the electrode surface on the characteristics of the double layer and on the adsorption of molecules and ions;

(2) the influence of the nature of the metal and of the chemisorption of solvent molecules (particularly water) on the structure of the interface and on adsorption;

(3) the dependence of the characteristics of the cathodic evolution of hydrogen on the nature of the metal and the structure of the double layer.

II. THE INFLUENCE OF THE CRYSTALLOGRAPHIC STRUCTURE OF THE ELECTRODE SURFACE ON THE PROPERTIES OF THE ELECTRICAL DOUBLE LAYER AND ON ADSORPTION

The vast majority of the literature data concerning the structure of the electrical double layer and adsorption on solid metals refer to electrodes with a polycrystalline surface. Measurements on individual faces of a single crystal are associated mainly with the determination of the zero-charge potential $\varphi_{\epsilon=0}$ of the face. The characteristics of the adsorption of ions and molecules on single crystal faces have been studied quantitatively on zinc[20,21], bismuth[22], gold[23], and silver[24]. Nevertheless the experimental data which have accumulated indicate an appreciable influence of the crystallographic characteristics on the double layer parameters. It has been established in studies on zinc[20,21,25] and bismuth[26-30] that the role of the nature of the polycrystallinity of the surface is manifested particularly clearly in the adsorption of organic compounds with a powerful attraction interaction in the adsorption layer.

In the study of the adsorption of pyridine[26], certain aliphatic ketones[27], esters[28], and camphor[29] on a surface-fused bismuth electrode the phenomenon of the splitting of adsorption–desorption maxima has been observed (Fig. 2). Such phenomena, which have been noted in many instances also on the polycrystalline surface of zinc[20,21,25], are absent from the homogeneous mercury surface and the (111) face of a bismuth single crystal. According to data for bismuth, the adsorption of pyridine and the majority of the ketones and esters investigated is accompanied by the splitting of the cathodic maxima into two, which is more pronounced the higher the concentration of the organic substance in solution. There are actually three peaks on the C–φ curves for propyl acetate solutions. The anodic maxima, which are obtained only for bismuth among solid metals, exhibit a smaller tendency towards splitting; the splitting of the anodic peaks into two components has been observed only for the adsorption of propyl acetate[28] and camphor[29] on bismuth.

As for the zinc electrode, the splitting of the adsorption maxima on bismuth is due to the polycrystallinity of the electrode, the surface of which comprises faces with different crystallographic indices. The individual narrow peaks in the region of the adsorption–desorption maxima (Fig. 2) describe the desorption of organic molecules from different single crystal faces, one of which is the (111) face. Presumably the difference between the values of $\varphi_{\epsilon=0}$ on different single crystal faces is the main factor among several responsible for the splitting of the maxima. The value of $\varphi_{\epsilon=0}$ for the basal (111) face of the bismuth single crystal in potassium sulphate solution is −0.68 V relative to the saturated calomel electrode[31], i.e. it is more negative by 30 mV than $\varphi_{\epsilon=0}$ for a surface-fused electrode[10,32]. On the basis of the value of $\varphi_{\epsilon=0}$ for the (111) face, the values of $\varphi_{\epsilon=0}$ for the remaining two faces involved in adsorption measurements can be estimated approximately from the peak potentials. $\varphi_{\epsilon=0}$ for the face corresponding to the first, i.e. least cathodic, peak of the split propyl acetate maximum is between −0.62 V and $\varphi_{\epsilon=0}$ for the face corresponding to the middle peak is in the range between −0.63 and −0.65 V.[30] However, it must be emphasised that the values quoted are merely approximate and do not permit the identification of the face.

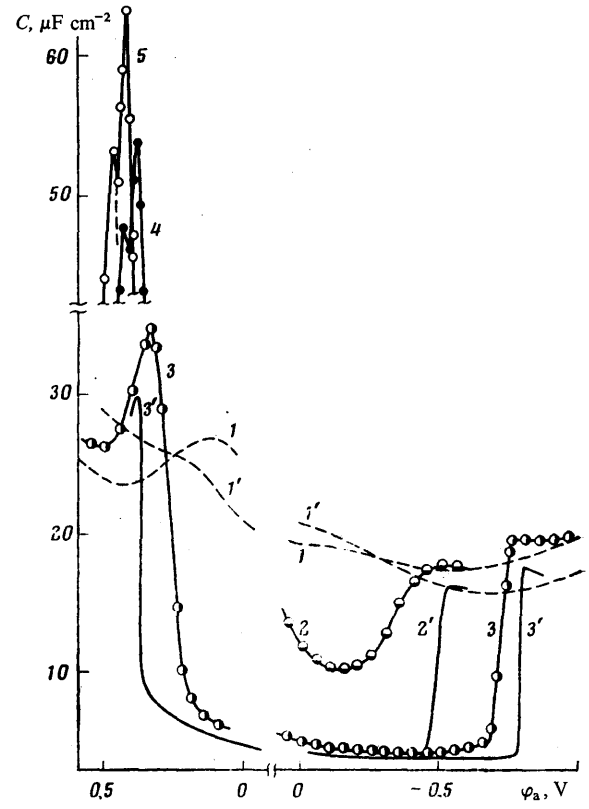

Figure 2. Differential capacitance curves for bismuth (curves *1* and *5*) and mercury (curves *1′* and *3′*) in 0.1 M NaF (bismuth and mercury) and $HClO_4$ (bismuth) solutions with added camphor; camphor concentration (M): 1) and 1′) 0; 2) and 2′) 2×10^{-4}; 3) and 3′) 1.5×10^{-3}; 4) 5×10^{-3}; 5) 7×10^{-3} (the potentials are given relative to the zero-charge point).

Electron-diffraction analysis has established that the splitting of the adsorption maxima is favoured by the macroscopic nature of the crystallographic heterogeneity of the surface of the bismuth electrode, characterised by

the presence on the surface of relatively large single-crystal sections[28-30]. The highly developed polycrystallinity and the associated appreciable energy inhomogeneity promote the manifestation of a broad spectrum of interactions in the adsorption layer, which leads to the spreading of the maxima and not to their splitting[25,30]. Mathematical analysis of electron diffraction patterns showed that, on a completely smooth bismuth surface produced by surface fusion (characterised by greatly extended reflections), there are relatively large single-crystal regions with the Miller indices (100), (101), (111), and (211).[30] Together with macroscopic single-crystal planes, one sometimes encounters aggregates of single crystals comprising between two and four crystallites with the indices (100), (111), (101), (552), (321), etc. Statistical treatment of the electron-diffraction data showed that the surface of the surface-fused bismuth drop comprises mainly two–three distinct single-crystal faces (the fraction of the total drop surface corresponding to them is about 80–90%). The crystallographic structure of the surface produced by partial fusion is statistically reproducible in different experiments owing to the stability of the conditions employed in the preparation of bismuth electrodes[10,11].

III. THE INFLUENCE OF THE NATURE OF THE METAL AND THE CHEMISORPTION OF SOLVENT MOLECULES ON THE STRUCTURE OF THE INTERFACE

Frumkin and coworkers[33,34] showed for the first time that the influence of the nature of the metal on the structure of the double layer and adsorption can be shown very clearly in terms of its hydrophilic properties. In particular, it has been established that, owing to the strong chemisorption of water molecules, the classical theory of the double layer is inapplicable to the double layer on gallium[35].

According to the literature data, in the region where $\epsilon \geq 0$ the adsorption parameters of organic compounds and ions depend markedly on the nature of the metal, owing to both their different hydrophilic properties and to the specific interaction of the functional group in the adsorbate molecule with the electrode surface. Table 1 presents the standard free energies of adsorption ΔG°_{A} of aliphatic alcohols, acids, and ketones, on mercury[36-38] and bismuth[27,39,40]. It is seen that the values of $-\Delta G^{\circ}_{A}$ for the higher members of the homologous series of the above compounds on bismuth are somewhat lower than on mercury. Since the functional group in the molecules of the higher homologues is so remote from the electrode surface that its specific interaction with the electrode may be neglected, the above difference is a result of the difference between the water adsorption energies on bismuth and mercury. Comparison of the values of $-\Delta G^{\circ}_{A}$ for different compounds shows that the energy of adsorption of water molecules on bismuth is on average 0.3–0.4 kcal mole^{-1} higher than on mercury. On the other hand, comparison of data for the adsorption of alcohols on bismuth and cadmium[41] shows that the energy of adsorption of water on bismuth is lower by 0.35–0.45 kcal mole^{-1} than on cadmium.

The relatively higher free energies of adsorption of the first members of the homologous series on bismuth compared with mercury are due to the appreciable specific interaction of the oxygen atoms in the functional group with the bismuth surface. The difference between the specific interactions of the functional groups with bismuth and mercury can be characterised by the quantity

$$[(-\Delta G^{0}_{A})_{n=6} - (-\Delta G^{0}_{A})_{n=2}]_{Hg} - [(-\Delta G^{0}_{A})_{n=6} - (-\Delta G^{0}_{A})_{n=2}]_{Bi} = (\Delta\Delta G^{0}_{A}).$$

Table 1 shows that the energy of interaction of the OH group with bismuth is 0.31 kcal mole^{-1} higher and that of the COOH group 0.60 kcal mole^{-1} higher than with mercury. It is interesting to note that the oxygen atoms in water and alcohol molecules interact with the bismuth surface approximately to the same extent. The stronger interaction of the COOH group with the electrode surface compared with the OH group is due to the face that the carboxy-group contains two oxygen atoms. The behaviour indicated by Table 1 has been confirmed also by comparing the adsorption activities of aliphatic compounds on bismuth and on the free surfaces of the solution[27,42,43].

Table 1. Standard free energies of adsorption of aliphatic compounds.

Compound	$(-\Delta G^{0}_{A})_{Hg}$, kcal mole^{-1}	$(-\Delta G^{0}_{A})_{Bi}$, kcal mole^{-1}	$(-\Delta G^{0}_{A})_{Hg} - (-\Delta G^{0}_{A})_{Bi}$, kcal mole^{-1}
C_2H_5OH	1.86	1.87	−0.01
C_3H_7OH	3.05	2.65	0.40
C_4H_9OH	3.83	3.47	0.36
$C_5H_{11}OH$	4.58	4.26	0.32
$C_6H_{13}OH$	5.39	5.09	0.30
$(-\Delta G^{0}_{A})_{n=6} - (-\Delta G^{0}_{A})_{n=2}$*	3.53	3.22	0.31
C_2H_5COOH	3.1	3.3	−0.2
C_3H_7COOH	3.8	3.7	0.1
C_4H_9COOH	4.55	4.4	0.15
$C_5H_{11}COOH$	5.55	5.1	0.45
$C_6H_{13}COOH$	6.3	5.9	0.4
$(-\Delta G^{0}_{A})_{n=6} - (-\Delta G^{0}_{A})_{n=2}$	3.2	2.6	0.6
Ethyl methyl ketone	—	3.55	—
Methyl propyl ketone	4.7	4.3	0.4
Butyl methyl ketone	5.35	5.00	0.35

*n is the number of carbon atoms in the hydrocarbon group.

The adsorption data obtained make it possible to establish a series of surface activities of aliphatic compounds reflecting the interaction of the functional group with the electrode surface. Judging from the values of ΔG°_{A}, the interaction of the functional group with the bismuth surface becomes stronger in the sequence OH < C=O < COOH.[29,44] This sequence reflects the enhancement of the specific interaction between the oxygen atoms and the bismuth surface.

The π-electron interaction between the aromatic ring and the positive surface charges, which should depend in principle on the nature of the metal, is known to play a significant role in the adsorption of aromatic compounds on electrodes. Table 2 presents the values of the adsorption energy gain $-\Delta G_{A}$ on passing from the solution/air interface to the interface with bismuth or mercury for $\Delta\sigma = 0.5$ μJ cm^{-2}.[45] The data in Table 2 show that the adsorption of all aromatic compounds on the bismuth surface is energetically more favourable than on the free surface of the solution. According to the Table, the values of $-\Delta G_{A}$ for mercury are 0.3–1.3 kcal mole^{-1} higher than for bismuth.

As shown above, one of the causes of the increased surface activity of organic compounds on bismuth is a

stronger adsorption of water molecules than on mercury. Together with this, it is necessary to take into account also the semimetallic nature of bismuth, which leads to a weakening of the π-electron interaction between adsorbate molecules and the surface. The energy of the π-electron interaction between the adsorbed molecules of benzene derivatives and an uncharged bismuth surface can be estimated approximately by comparing the values of $-\Delta G_A$ for phenol and cyclohexanol. According to the data in Table 2, the difference between the values of $-\Delta G_A$ for phenol and cyclohexanol (0.7 kcal mole^{-1}) characterises the energy of the π-electron interaction of benzene derivatives; however, depending on the nature and structure as well as the orientation of the adsorbed molecules, this value can vary somewhat. The energy of the additional π-electron interaction when the molecule includes a second benzene ring (naphthalene derivatives) appreciably exceeds the energy of the interaction of the functional group (OH, NH_2, etc.) with the bismuth surface.

Table 2.

Compound	$-\Delta G_A$, kcal mole^{-1}		Compound	$-\Delta G_A$, kcal mole^{-1}	
	Bi	Hg		Bi	Hg
Phenol	1.0	1.8	o-Toluidine	1.5	2.2
Cyclohexanol	0.3	—	Pyridine	0.6	0.9
Catechol	1.8	2.7	Benzene	0	0.5
Hydroquinone	2.8	3.7	Toluene	0.4	0.7
o-Cresol	1.3	—	Naphthalene	2.2	—
Benzyl alcohol	1.3	—	α-Naphthol	3.9	—
Benzoic acid	1.3	1.74	α-Naphthylamine	3.6	—
Aniline	1.2	2.5	α-Naphthoic acid	3.6	—

The difference between the adsorption behaviour of organic compounds on mercury and bismuth becomes appreciably enhanced for high positive surface charges. Experimental data have shown that anodic adsorption–desorption maxima for aliphatic compounds on bismuth are displaced by 0.1–0.15 V towards less positive values of φ than on mercury[27–29,39–45]. The main cause of this effect is the appreciable intensification of the chemisorption of water molecules with increase of ϵ on bismuth[46].

An important result of the different hydrophilic properties of metals and of different interactions of the functional group with the electrode surface in the adsorption of organic compounds is appreciable differences in the orientation of the adsorbate molecules in the adsorption layer[27–29,39–45]. On a bismuth electrode, organic compounds are oriented more vertically in the adsorption layer than on the mercury surface. The differences between the orientations of the adsorbed molecules are clearly shown in the adsorption of coumarin on bismuth and mercury. Coumarin molecules are adsorbed on mercury[47] and bismuth[48] in two different positions: in the vertical position at $\epsilon < 0$ and in an inclined position near $\varphi_{\epsilon=0}$. Fig. 3 shows that the regions corresponding to the adsorption of coumarin on mercury in the two positions are separated by narrow reorientation peaks; on the other hand, there is virtually no reorientation maximum on bismuth. Theoretical analysis of experimental C–φ curves for the adsorption of coumarin, based on the model of three parallel condensers, showed that the orientation of coumarin molecules in the adsorption layer on bismuth is appreciably more vertical than on mercury, as a result of which the attraction interaction between the horizontally and vertically oriented molecules on bismuth is much stronger than on mercury[48].

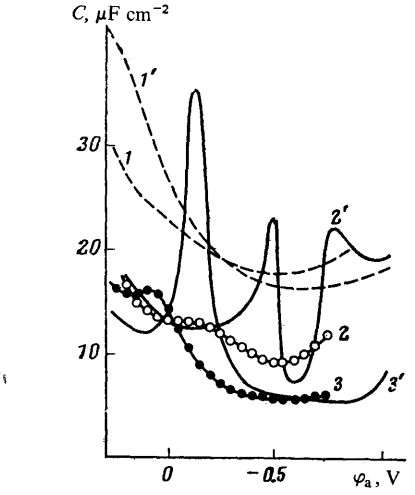

Figure 3. Differential capacitance curves for bismuth (curves *1–3*) and mercury (curves *1′–3′*) in 1 *N* potassium sulphate (bismuth) and sodium sulphate (mercury) solutions with added coumarin; coumarin concentration (M): 1) and 1′) 0; 2) and 2′) 7×10^{-4}; 3) and 3′) 5×10^{-3} (the electrode potentials were measured relative to the zero-charge point.

Although there are few literature data on the structure of the electrical double layer in non-aqueous solvents, nevertheless one might assert that the specific interaction of solvent molecules with the metal surface in the dense layer is manifested also in non-aqueous solvents.

Table 3.

Solvent	$\Delta\varphi^{Bi-Hg}_{\epsilon<0}$, V	$\Delta\varphi^{Bi-Hg}_{\epsilon=0}$, V	$\Delta\varphi^{Bi-Hg}_{\epsilon<0} - \Delta\varphi^{Bi-Hg}_{\epsilon=0}$, V	Electrolyte
Water	−0.145	−0.190	−0.045	0.1 *N* Na_2SO_4
Methanol	−0.14	−0.18	−0.04	0.1 *M* NH_4F
Acetonitrile	−0.13	−0.16	−0.03	0.1 *M* $NaClO_4$
Dimethyl-formamide	−0.14	−0.25	−0.11	0.1 *M* $NaClO_4$
Dimethyl sulphoxide	−0.09	−0.15	−0.06	0.1 *M* $LiClO_4$

Table 3 presents the differences between the zero-charge potentials on mercury and bismuth ($\Delta\varphi^{Bi-Hg}_{\epsilon=0}$) and the potential differences at a constant high negative charge ($\Delta\varphi^{Bi-Hg}_{\epsilon=0}$) for various non-aqueous solvents[19]. The latter differences should depend relatively little on the nature of the solvent[34,49].

The data in Table 3 show that the values of $\Delta\varphi^{Bi\text{-}Hg}_{\epsilon \ll 0}$ (for $\epsilon = -10 - -17 \mu C\ cm^{-2}$) depend comparatively little on the nature of the solvent, while the dependence of $\Delta\varphi^{Bi\text{-}Hg}_{\epsilon = 0}$ is appreciably greater. Evidently in all the solvents investigated the preferential orientation of the dipoles with the negative ends towards the metal surface at $\epsilon = 0$ is somewhat more pronounced on bismuth than on mercury. Particularly notable effects are observed in dimethylformamide (DMF) and dimethyl sulphoxide (DMSO). Comparison of the $\epsilon - \varphi$ curves for mercury and gallium or an indium–gallium alloy showed that near $\varphi_{\epsilon = 0}$ for gallium or an indium–gallium alloy DMSO molecules are clearly oriented with the negative end of the dipole towards the electrode surface[49]. On the other hand, in acetonitrile the specific interaction between the acetonitrile dipoles and gallium or an indium-gallium alloy is extremely weak.

Table 4. The adsorption equilibrium constants.

Solvent / ion	H_2O	CH_3OH	C_2H_5OH	DMF	Acetonitrile
Na^+	−9	—	—	—	—
K^+	−7	−2.6	−5.0	—	—
NH_4^+	−6.7	—	—	−17.5	—
Rb^+	−3.8	−2.1	—	−14.3	—
Cs^+	−1.4	−1.6	—	−11.5	—
Cl^-	1.75	4	4.5	11.6	—
Br^-	4.5	6.1	—	12.5	11.1
I^-	8.1	10.4	11.7	14.0	14.7
I^- on (111) face	8.8	—	—	—	—
SCN^-	5.2	5.3	5.9	6.4	5.6
NO_3^-	0.4	—	—	3.2	—

The nature of the solvent has an appreciable influence on the adsorption of ions on electrodes. The most systematic data for the adsorption of ions from non-aqueous solvents are available for the bismuth electrode[17,19,50–56]. Table 4 presents the adsorption equilibrium constants ($\ln\beta_{\epsilon = 0}$), referring to the virial isotherm, for various ions on bismuth.

Evidently the free energy of adsorption depends very strongly on the nature of the surface-active ion, and increases greatly on passing from cations to anions. Among alkali metal cations, Cs^+ and Rb^+ exhibit the highest surface activity, while the remaining cations are adsorbed much more weakly.

The significant difference between the free energies of adsorption of cations and anions shows that different types of forces are responsible for the specific adsorption of the two types of species. For a given ion, the free energy of adsorption depends significantly on the nature of the solvent. In the adsorption of cations from protic solvents (water and alcohols) the values of $\ln\beta_{\epsilon = 0}$ are higher by several orders of magnitude than for adsorption from aprotic solvents (DMF). The main cause of this effect is the appreciable enhancement of the solvation of cations on passing to aprotic solvents[57]; the different energies of interaction of the corresponding solvent molecules with the electrode surface also play a definite role. The opposite phenomenon occurs in anion-active systems—the free energy of adsorption increases appreciably (with the exception of the SCN^- anion) on passing from protic to aprotic solvents, which is mainly associated with the weakening of the solvation of anions in aprotic solvents[57]. As a result of the weakening of the solvation of halides, in the series $I^- > Br^- > Cl^-$, aprotic solvents lead to the equalisation of the free energies of adsorption.

Judging from the available literature data[53], the free energy of adsorption of cations depends little on the nature of the electrode. On the other hand, the free energy of adsorption of anions on bismuth in aqueous and alcoholic solutions is appreciably lower than on mercury. In DMF (there are no data for mercury in acetonitrile) the energy of adsorption of anions on bismuth[56] is virtually the same as on mercury[58].

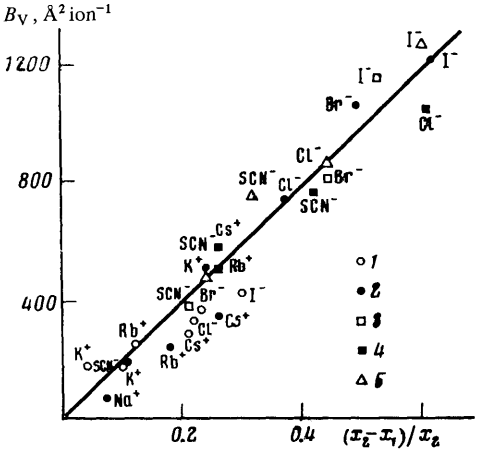

Figure 4. Variation of the second virial coefficient with the ratio $(x_2 - x_1)/x_2$ for different ions in different solvents: 1) water; 2) methanol; 3) acetonitrile; 4) dimethylformamide; 5) ethanol.

The nature of the solvent has a significant influence on the repulsion interaction between specifically adsorbed ions. It has been established for the bismuth electrode that the repulsion interaction is enhanced for a given ϵ = const., both with increase of the radius of the ions and with increase of the dimensions of the molecules of the solvent. Fig. 4 compares the second virial coefficients B with the ratios $(x_2 - x_1)/x_2$†.[17,51] To a first approximation, the relation illustrated in Fig. 4 may be regarded as linear; it suggests that the repulsion interaction of the adsorbed ions increases almost in proportion to the distance of the plane containing the charge centres of the specifically adsorbed ions from the outer Helmholtz plane. This relation can be accounted for qualitatively by the weakening of the screening effect of the diffuse layer on the repulsion between the specifically adsorbed ions with increase of the distance $x_2 - x_1$.[17,51,58,59]

IV. THE INFLUENCE OF THE STRUCTURE OF THE ELECTRICAL DOUBLE LAYER ON THE KINETICS OF THE CATHODIC EVOLUTION OF HYDROGEN

Kinetic studies have shown that surface-fused solid electrodes are the most suitable objects for the quantitative study of electrode reactions, particularly the cathodic

† x_1 and x_2 are the distances of the inner and outer Helmholtz planes from the electrode surface respectively.

evolution of hydrogen. When the surface of the metal is fused in an inert atmosphere, a stable state of the surface layer of metal is achieved and the occurrence of certain side reactions (the incorporation of cations from an alkaline solution), which greatly hinder the study of the true kinetics of hydrogen evolution, is strongly inhibited on electrodes of this kind[60].

Owing to the relatively high hydrogen overvoltage and the negative potential $\varphi_\epsilon = 0$, metals such as bismuth, tin, lead, and cadmium are suitable for the investigation of the influence of the structure of the electrical double layer on the rate of evolution of hydrogen in the region of polarisations close to $\varphi_\epsilon = 0$, where double layer effects should be manifested most clearly. According to the equation proposed by Frumkin on the basis of the theory of the slow discharge of H_3O^+,

$$\eta = a + \frac{1-\alpha}{\alpha}\psi_1 - \frac{1-\alpha}{\alpha}\frac{RT}{F}\ln c_{H_3O^+} + \frac{RT}{\alpha F}\ln i, \qquad (1)$$

the overvoltage η for a constant composition of the solution is influenced not only by the change in current density i, but also by the change in the ψ_1 potential. In Eqn. (1) a is a constant, α the transfer coefficient, and F the Faraday.

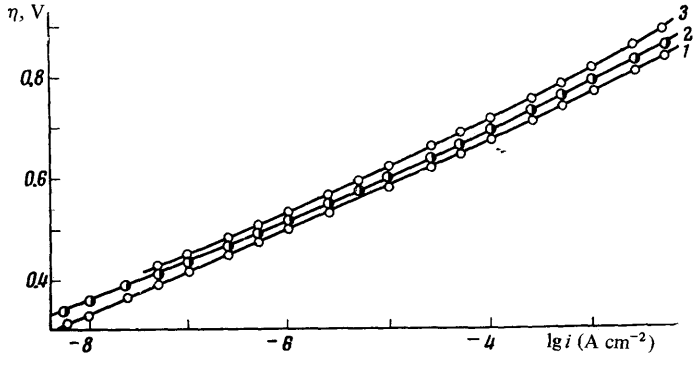

Figure 5. Polarisation curves for the evolution of hydrogen on bismuth in different solutions: 1) 1 N $HClO_4$; 2) 0.1 N $HClO_4$; 3) 0.1 N $HClO_4$ + 0.9 N $LiClO_4$.

Measurements on bismuth have shown that, in highly purified solutions (complete elimination of oxygen and of traces of other depolarisers), the variation of η with $\lg i$ in solutions of surface-inactive electrolytes is described by smooth curves without any sharp jumps in both aqueous[61,62] and methanol[63] media (Fig. 5). The low slopes of these curves, which depend on the acid concentration $c_{H_3O^+}$ and on η, are caused both by the change in the diffuseness of the double layer with electrode potential and electrolyte concentration and by the fact that the coefficient α for the hydrogen evolution reaction on bismuth exceeds 0.5.[61,62]

Using the values of ψ_0 instead of ψ_1 (this is justified to a first approximation for surface-inactive electrolytes), corrected Tafel relations (c.t.r.) were plotted for the hydrogen evolution reaction on bismuth. Such relations in 0.1 and 1.0 M $HClO_4$ solutions are linear over a wide range of potentials (Fig. 6). The results show that α is independent of acid concentration and amount to 0.61 ± 0.01. The higher value of the coefficient α was confirmed in a study of the dependence of η on $c_{H_3O^+}$ at a constant overall electrolyte concentration with the coefficient $(\partial\eta/\partial \ln c_{H_3O^+})_c = -36$ mV and also in the determination of the change in η caused by the increase of the overall electrolyte concentration $c_{H_3O^+}$ = const.

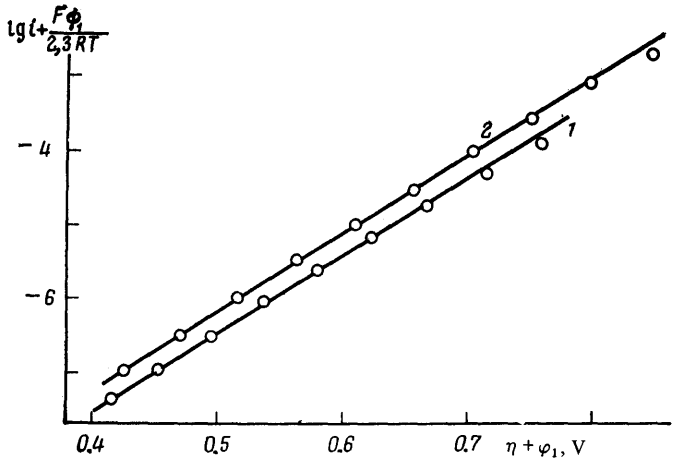

Figure 6. Corrected Tafel relations for the cathodic evolution of hydrogen on bismuth in $HClO_4$ solutions (N): 1) 1.0; 2) 0.1.

It has been shown[64] that, when the fundamental postulates of the diffuse layer theory and the double layer model proposed by Gram in the absence of specific adsorption are used, the slope of the η–$\lg i$ curve can be calculated from the formula

$$b_{theor} = \left[\frac{\alpha F}{RT} + \frac{2(1-\alpha)C_G}{\sqrt{4A^2c + \epsilon^2} + \frac{2RT}{F}C_G}\right]^{-1}, \qquad (2)$$

where C_G is the capacitance of the dense layer and $A = \sqrt{DRT/2\pi}$ (D is the dielectric constant). Comparison of the experimental coefficients b with b_{theor} in 0.1 M $HClO_4$ solutions corresponding to different values of η for bismuth shows that, when $\eta < 0.8$ V, the agreement between experiment and calculation is extremely satisfactory. The significant discrepancies between the values of b for $\eta \geq 0.8$ V are probably caused by the specific properties of bismuth (metallisation) and are not related to the inaccuracy of Eqn. (2).[64]

Quantitative analysis of kinetic and capacitance data in terms of the model ideas developed by Krishtalik[65] showed that in the case of bismuth a fraction of the overall potential jump at the interface corresponds to the metallic phase[66]. It has been suggested that the decrease of α for $\eta \geq 0.8$ V ($\epsilon \gg 0$) is due to the metallisation of bismuth[29]. This hypothesis has been confirmed in a study of the chemisorption of water on bismuth[67].

Data similar to those quoted above were also obtained in a study of the kinetics of the evolution of hydrogen in the region of $\varphi_\epsilon = 0$ on gallium, indium, and their amalgams at elevated temperatures[68-71]. On the other hand, at room temperature the slope of the η – $\lg i$ curves for gallium[72], tin[73], and cadmium[14] proved to be virtually

independent of η, although the values of $\varphi_{\epsilon=0}$ for these metals are in the range of i accessible to measurement. The causes of such phenomena on cadmium and tin have not been established; they are probably associated with the enhanced hydrophilic properties of these metals[14,72].

Direct study of the kinetics of the cathodic evolution of hydrogen in an alkaline medium is possible on electrodes smoothed by surface fusion, because there is virtually no incorporation of alkali and alkaline earth metals into such electrodes owing to the comparatively overvoltage for such incorporation[60]. It has been found that the evolution of hydrogen on antimony[12,74], tin[75], and cadmium[14] electrodes takes place in alkaline solutions of different compositions via the mechanism involving the slow discharge of protons derived from water molecules. This mechanism was proposed for the first time by Frumkin and coworkers[76] for the nickel electrode as early as 1939.

Alkali and alkaline earth metal cations in solution exhibit an accelerating effect on the rate of evolution of hydrogen, which in the case of tin increases in the series from Li^+ to Cs^+ and from Ca^{2+} to Ba^{2+}.[75] In interpreting this effect, use was made of the hypotheses of both the specific adsorption of cations and of the involvement in the discharge process of the water molecules in the hydration shells of the cations[75,77]. As regards the influence of cations on η in an alkaline medium, there is a similarity between tin on the one hand and antimony[12,74] and cadmium[14] and partly liquid gallium[78] and saturated indium amalgam[77,79] on the other. The evolution of hydrogen on pure mercury in alkaline solutions is known to proceed via a mechanism different from that described above[79,80].

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Adsorption Phenomena on Platinum Group Metal Electrodes

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Certain fundamental concepts and definitions in the thermodynamic theory of the platinum electrode are examined and the concepts of the zero total charge and zero free charge potentials and methods for determination of these quantities are discussed. Data indicating charge transfer in chemisorption processes are analysed and a thermodynamic approach to the analysis of this phenomenon is considered. The influence of the pH of the solution on the structure of the platinum metal-electrolyte solution interface is examined.
The bibliography includes 186 references.

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I. INTRODUCTION

The study of the structure of the platinum metal–electrolyte solution interface was begun by Frumkin and coworkers at the end of the 1920s and the beginning of the 1930s.[1-8] They developed methods for the measurement of charging and adsorption curves, laid the foundations of the thermodynamic theory of surface phenomena on platinum metals, and formulated the fundamental idea of a close relation between the adsorption of ions in solution and the adsorption of hydrogen and oxygen atoms. Subsequently the Soviet electrochemical school made a significant contribution to the study of the above interface, which has been reflected in a number of reviews[9-13]. Some of the main results obtained in the last 10–15 years are discussed in the present review. The considerable attention devoted to the adsorption properties of platinum metals during this period is due to attempts at devising fuel cells and the extensive development of research on liquid-phase catalytic hydrogenation and oxidation reactions and electrosynthetic processes.

One of the characteristic features of the development of such studies in recent years is the increased number of systems investigated. Together with a further deepening of the investigation of the adsorption properties of the platinum electrode, measurements have also been made on other platinum metals and their alloys (on smooth polycrystalline and single-crystal electrodes, on electrolytic deposits of platinum metals, on metal blacks, and on deposited catalysts).

A second noteworthy characteristic feature is the wide range of experimental techniques which have been used in the investigation of adsorption phenomena on platinum group metals. Thus the method of radioactive tracers[14-16] has been significantly improved, which made it possible to increase the accuracy and reliability of the results obtained by this method and extended its scope, particularly in the study of the kinetics of adsorption and of the exchange of adsorbed ions with ions in the solution. The potentiodynamic method and potentiostatic pulse methods for the investigation of adsorption have been appreciably expanded and developed[17-23]. A series of adsorption studies has been carried out by the two-electrode thin-layer method[24-48]. New information about the state of the surface layer on platinum metals has been provided by the method involving the measurement of estance[49-66]. The method of the rotating disc electrode with a ring has been used to investigate the adsorption and anodic elimination of adsorbed species[67-78]. Attempts have been made at a detailed study of the surface properties of platinum metals with the aid of optical methods (ellipsometry, electroreflectance)[79-86] and by measuring the electrical resistance of thin metallic films sputtered *in vacuo* on to a non-conducting base[87-95].

II. SOME CONCEPTS AND RELATIONS OF THE THERMODYNAMIC THEORY OF THE PLATINUM ELECTRODE

The third characteristic feature of the period under consideration is the application of the thermodynamic theory of the reversible electrode in the interpretation of the behaviour of platinum metals in electrolyte solutions. This theory was outlined by Frumkin and coworkers[7-9], was applied by them for the first time in a later study[96], and was subsequently developed further[97-124]. The last series of studies was stimulated directly by the derivation[97] of an equation which made it possible to carry out a comparatively simple experiment test of the applicability of the Gibbs adsorption equation to platinum metals. Such a test for 30 different systems comprising platinum[98,99,101,105,109,110,112,125], palladium[126], rhodium[100,101,104,111], iridium[108,111,115], ruthenium, and platinum–ruthenium[101,103] electrodes showed that the thermodynamic theory is applicable not only at potentials in the hydrogen and "double layer" regions, but also in the initial section of the region corresponding to the adsorption of oxygen on the electrodes. The pronounced phenomena associated with the chemisorption of ions from solution result in a narrowing of the region of practical applicability of the theory.

The thermodynamic theory led to the development of the method of isoelectric potential shifts[98,99] (the first measurements of the shifts of the potential of an isolated

electrode following the alteration of the pH of the solution were undertaken in early investigations[7,8]). A potentiometric titration procedure for a constant total surface charge, which made it possible to investigate the adsorption properties of platinum and rhodium in the range of intermediate pH value which had been previously inaccessible to experimental study[128-131], was developed recently[127].

In the experimental test of the thermodynamic theory in solutions of acids HA with an excess of the neutral salt CA $\{[HA] \ll [CA]\}$ the following relation was used:

$$(\partial\varphi_r/\partial\mu_{H^+})_{\Gamma_H,\mu_{CA}} = (\partial\Gamma_{H^+}/\partial\varphi_r)_{\mu_{H^+},\mu_{CA}}/(\partial\Gamma_H/\partial\varphi_r)_{\mu_{H^+},\mu_{CA}}, \quad (1)$$

where φ_r is the potential relative to the reversible hydrogen electrode in the same solution, μ_{H^+} and μ_{CA} are the chemical potentials of hydrogen ions and the salt, and Γ_H and Γ_{H^+} are the Gibbs adsorptions of hydrogen atoms and ions respectively. All the quantities in Eqn. (1) are expressed in electrical units. This equation is valid also for solutions of neutral salts which have been made alkaline. The term "isoelectric potential shift" (introduced for the first time by Ponomarenko et al.[132]) was proposed for the quantity $(\partial\varphi_r/\partial\mu_{H^+})_{\Gamma_H,\Gamma_{CA}}$. The Gibbs adsorptions Γ_H and Γ_{H^+} represent the amounts of the corresponding components which must be introduced into the system for their chemical potentials to remain unchanged without the supply of electricity from the outside when the surface area of the electrode is increased by 1 cm^2. Evidently the electrode potential also remains constant under these conditions. The Gibbs adsorptions must be distinguished from the excess surface amounts, which are designated by A_H and A_{H^+} respectively. The relations between Γ_H and A_H and between Γ_{H^+} and A_{H^+} are

$$\Gamma_H = A_H - \varepsilon, \quad (2)$$

and

$$\Gamma_{H^+} = \varepsilon + A_{H^+}, \quad (3)$$

where ϵ is the charge of the metallic component of the electrical double layer.

Whereas both Γ_H and Γ_{H^+} are thermodynamic quantities susceptible in principle to direct experimental determination, the introduction of the quantities A_H, A_{H^+}, and ϵ is associated with definite model assumptions. In particular, in the determination of A and ϵ no account is taken of the partial charge transfer via the Lorenz mechanism[133] for all the ions in the double layer. For strongly chemisorbed ions, it is almost impossible to determine ϵ unambiguously. In the presence of an excess of the salt in solution, hydrogen ions are displaced from the diffuse part of the double layer by the salt cation[113,134,135], so that $A_{H^+} = 0$ and $\Gamma_{H^+} = \epsilon$.

It has been shown[117-119] that $\Gamma = -Q'$ and $\Gamma_{H^+} = Q''$, where Q' and Q'' are the total surface charges, i.e. the amounts of electricity which must be introduced at μ_{H^+} = const. or μ_H = const. respectively in order to prevent a change in the composition of the bulk phase following an increase of the surface area of the electrode by 1 cm^2 when the loss of material is compensated by the introduction of an amount of substance $\Gamma_H + \Gamma_{H^+} = A_H + A_{H^+}$ (H in the former case and H^+ in the latter case). Henceforth the symbol Q will be used for Q' and this quantity will be called the total charge (the condition μ_{H^+} = const. is omitted for brevity). Instead of Q'', the symbol Γ_{H^+} will be empoyed; in order to distinguish this total charge from Q, we shall adopt the term free charge for Γ_{H^+}.

III. CHARGING CURVES OF THE FIRST AND SECOND KINDS

According to the general concept of the electrode charge, there should exist two types of charging curve for platinum metals. The usual charging curve, characterising the relation between the total charge Q and the potential φ at a constant chemical potential of hydrogen ions (μ_{H^+} = const.) may be called the charging curves of the first kind. Since according to the literature[117,119]

$$(\partial\sigma/\partial\varphi_A)_{\mu_{HA},\mu_{CA}} = \Gamma_H = -Q, \quad (4)$$

where σ is the amount of reversible surface work and φ_A the potential referred to an electrode reversible with respect to the anion, integration of charging curves of the first kind makes it possible to determine the electrocapillary curves of the first kind (to within an integration constant). Accordingly, the derivative $(\partial Q/\partial\varphi)_{\mu_{H^+},\mu_{CA}} = -(\partial\Gamma_H/\partial\varphi)_{\mu_{H^+},\mu_{CA}} = C$ may be called the differential capacitance of the first kind. In the literature this quantity is usually referred to as the polarisation capacitance or the total capacitance of the electrode.

Charging curves of the second kind represent the relation between the total charge Γ_{H^+} and the electrical potential corresponding to a constant chemical potential of hydrogen μ_H = const. (φ_r = const.). Since

$$(\partial\sigma/\partial\varphi_A)_{\mu_H,\mu_{CA}} = -\Gamma_{H^+}, \quad (5)$$

integration of charging curves of the second kind leads to electrocapillary curves of the second kind. The quantity $(\partial\Gamma_{H^+}/\partial\varphi)_{\mu_H,\mu_{CA}}$ may be called the differential capacitance of the second kind. In a solution containing an excess of an extraneous inactive electrolyte, it can be set equal to the equilibrium capacitance of the electrical double layer.

The methods for the measurement of the usual charging curves are generally known[9]. In order to find the charging curves of the second kind corresponding to φ_r = 0, a potentiometric titration method with a large indicator electrode has been employed[7,8,136,137]. Charging curves of the second kind for anodic values of φ_r have been obtained by intersecting a family of Γ_{H^+}–φ_r curves, obtained by potentiometric titration under isoelectric conditions, by vertical φ_r = const. lines[130,138]. These curves have a simpler shape than the usual charging curves corresponding to the condition μ_{H^+} = const., since the changes in the amounts of adsorbed hydrogen and oxygen at φ_r = const. are relatively small. The decrease of the slope of the curves with increasing φ_r is due to the transition from the region of adsorption of the cations to that of the anions.

IV. THE ZERO TOTAL CHARGE AND ZERO FREE CHARGE POTENTIALS

It follows from the general concept of electrode charge that there should exist zero total charge and zero free charge potentials for platinum metals. The potential at which the quantity $-\Gamma_H = Q = \epsilon - A_H$ becomes zero is called the zero total charge potential $\varphi_{Q=0}$ (z.t.c.p.). The potential at which the total charge Γ_{H^+} becomes zero in a solution with an excess of a neutral salt is called the zero free charge potential $\varphi_{\Gamma_{H^+}=0}$ (z.f.c.p.).

A method for determination of z.t.c.p. on the basis of the non-thermodynamic equation $Q = \epsilon - A_H$ has been

described[7,8,116] and the results of the determination of $\varphi_{Q=0}$ for platinum metals by this procedure are presented in Table 1. The highest anodic values of $\varphi_{Q=0}$ correspond to palladium and platinum. The $\varphi_{Q=0}$ shift in the negative direction with increase of the adsorbability of the anions of the solution and in the positive direction with increase of the adsorbability of the cations. It has been shown[115,124] that the method in which the surface of the electrode is scraped off in solution[139-142] should lead in principle to $\varphi_{Q=0}$ if an equilibrium is established during the scraping process between the electrode and the solution and the pH of the latter remains constant.

Table 1. Zero total charge potentials of platinum metals.

Solution	$\varphi_{Q=0}$, V (w.r.t. normal H e-de)	References
Platinum		
0.3 *N* HF+0.12 *N* KF (pH 2.4)	0.235	149
1 *N* Na_2SO_4+0.01 *N* H_2SO_4 (pH 2.4)	0.20	120
1 *N* KCl+0.01 *N* HCl	0.14	99
1 *N* KBr+0.01 *N* HBr	0.06	120
1 *N* Na_2SO_4+0.01 *N* NaOH	−0.25	120
1 *N* KCl+0.01 *N* KOH	−0.30	120
1 *N* KBr+0.01 *N* KOH	−0.33	120
1 *N* KI+0.01 *N* KOH	−0.48	120
0.01 *N* H_2SO_4+0.1 *N* Na_2SO_4+0.01 *N* $ZnSO_4$	0.29	166
Palladium		
0.1 *N* Na_2SO_4+0.002 *N* H_2SO_4	0.26	126
Rhodium		
0.3 *N* HF+0.12 *N* KF (pH 2.4)	0.085	149
1 *N* Na_2SO_4+0.01 *N* H_2SO_4	0.05	120
1 *N* KCl+0.01 *N* HCl	0.02	120
1 *N* Na_2SO_4+0.01 *N* NaOH	−0.40	120
Iridium		
1 *N* Na_2SO_4+0.01 *N* H_2SO_4	0.10	115
1 *N* KCl+0.01 *N* HCl	0.06	115
1 *N* KBr+0.01 *N* HBr	−0.03	115

The most reliable values of z.f.c.p. were obtained from direct measurements of the relation between Γ_{H^+} and φ_r or from measurements of the dependence of the adsorption of anions Γ_{A^-} and cations Γ_{C^+} on φ_r in solutions with an excess of the salt. In the second method, employed for the first time by Balashova and Merkulova[143], z.f.c.p. represents the potential at which $\Gamma_{A^-} = \Gamma_{C^+}$, since, by virtue of the electroneutrality condition, $\Gamma_{H^+} = \Gamma_{A^-} - \Gamma_{C^+}$. The values of z.f.c.p. found by the above method are listed in Table 2. The z.f.c.p. shift in the negative direction along the series Pt > Pd > Rh > Ir > Ru and are less positive than the z.t.c.p. Both z.t.c.p. and z.f.c.p. shift in the negative direction in the presence of specifically adsorbably anions and in the positive direction in the presence of specifically adsorbable cations.

In solutions of a surface-inactive electrolyte, z.f.c.p. is the zero-charge potential of the double layer (z.c.p.) and is analogous to z.c.p. of metals which do not adsorb hydrogen and oxygen. The Li^+ and Na^+ cations and F^- anions are least adsorbable on platinum metals[144-149]. In the presence of these ions z.f.c.p. may be regarded as z.c.p. In other cases chemisorption bonds arise between the surface of the metal and the adsorbed ions, whose strength depends on the nature of the ion and the electrode and also on the potential and pH of the solution. As a result, there is a possibility of partial or even total transfer of the charge of the ion being adsorbed to the surface of the metal. The transition of ions undergoing adsorption to the atomic adsorbed state under the conditions of an "insufficient potential", i.e. up to potentials corresponding to equilibrium values, for example in metal–metal ion systems, has been recently investigated by a wide variety of methods[24-48,67-78,83,95,150,151]. Measurements of the superequivalent adsorption of anions on platinum (Fig. 1) and rhodium are instructive in this respect[152]. These measurements indicate an increase of the superequivalent adsorption of anions on platinum in the series $SO_4^{2-} < I^- < Cl^- < Br^-$ and on rhodium in the series $SO_4^{2-} < Br^- < Cl^-$. The anomalous positions of I^- and Br^- in these series and also the nature of the variation of the degree of adsorption of cations with potential for positive surface charges (Fig. 1) can be interpreted, provided it is assumed that the degree of charge transfer from the anions to the surface of the metal increases with increasing adsorbability of the anions and when the potential shifts towards anodic values.

Table 2. Zero free charge potentials of platinum metals.

Solution	$\varphi_{\Gamma_{H^+}=0}$, V (w.r.t. normal H e-de)	References
Platinum		
0.3 *N* HF+0.12 *N* KF (pH 2.4)	0.185	149
0.3 *N* Li_2SO_4+0.01 *N* H_2SO_4	0.16	113
1 *N* Na_2SO_4+0.01 *N* H_2SO_4	0.16	109
0.01 *N* $ZnSO_4$+0.1 *N* Na_2SO_4+0.01 *N* H_2SO_4	0.27	166
1 *N* KCl+0.01 *N* HCl	0.05	99
1 *N* KBr+0.01 *N* HBr	−0.03	109
1 *N* KBr+0.01 *N* KOH	−0.39	105
1 *N* KI+0.01 *N* KOH	−0.52	105
$4 \cdot 10^{-3}$ *N* + Na_2SO_4 pH 3÷6	0.13±0.02	168
Palladium		
0.1 *N* Na_2SO_4+0.002 *N* H_2SO_4 (pH 3)	0.10	126
Rhodium		
0.3 *N* HF+0.12 *N* KF (pH 2.4)	−0.005	149
1 *N* Na_2SO_4+0.01 *N* H_2SO_4	−0.04	104
1 *N* KCl+0.01 *N* HCl	−0.12	100, 101
Iridium		
0.3 *N* HF+0.12 *N* KF (pH 2.4)	−0.01	149
1 *N* Na_2SO_4+0.01 *N* H_2SO_4	−0.06	108
1 *N* KCl+0.01 *N* HCl	−0.13	108
1 *N* KI+0.01 *N* KOH	−0.59	
	0.06	115
Ruthenium		
1 *N* KCl+0.01 *N* HCl	0.50	103
Electrolytically mixed Pt-Ru deposit with 10 wt.% Ru		
1 *N* KCl+0.01 *N* HCl	−0.01	103

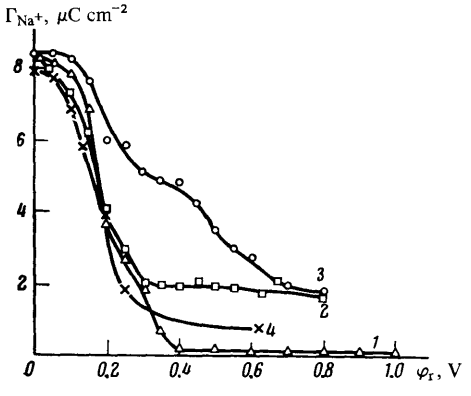

Figure 1. Variation of the degree of adsorption of sodium cations with the potential of a platinised platinum electrode in different solutions: 1) 0.003 *N* H_2SO_4 + 0.003 *N* Na_2SO_4; 2) 0.001 *N* HCl + 0.001 *N* KCl; 3) 0.001 *N* HBr + 0.003 *N* NaBr; 4) 0.001 *N* H_2SO_4 + 0.003 *N* NaI (according to the data of Kazarinov et al.[152]).

Owing to charge transfer, the definition of ϵ and the assumption that $\varphi\Gamma_{H^+}=0$ is equal to z.c.p. become arbitrary. For this reason, the quantity $\varphi\Gamma_{H^+}=0$, the physical significance of which is independent of the nature of the solution, may be regarded as equal to z.c.p. merely as a matter of convention in systems containing specifically adsorbable ions. The conventional nature of the concept of z.c.p. in the presence of strong specific adsorption can be clearly demonstrated[153] for a platinum electrode coated by adsorbed iodide and thallium ions. It has been shown that the position of z.c.p. depends on whether the adsorbed iodide and thallium ions become attached to the metallic or ionic components of the double layer.

V. FORMAL CHARGE TRANSFER COEFFICIENTS IN CHEMISORPTION PROCESSES

The problem of charge transfer in chemisorption processes has been recently discussed in detail[154-165]. It is noteworthy that the thermodynamic approach to charge transfer in the adsorption of hydrogen atoms on the surface of platinum was outlined in early investigations[7,8] in terms of the contributions of the hydrogen atom (X) and the double layer ion (Y), with the corresponding charge on the metal, to the potential jump at the electrode/solution interface. It has been shown[158,163] that chemisorption processes can be usefully characterised by formal charge transfer coefficients, which are referred to as such because they reflect not only the fraction of the charge transferred from the adsorbed species to the electrode but also the change in the parameters of the double layer caused by the adsorption process. In the adsorption of hydrogen atoms on the electrode surface the formal charge transfer coefficient n_2 may be calculated from the equation

$$n_2=(\partial\Gamma_{H^+}/\partial\Gamma_\Sigma)=-X/Y, \tag{6}$$

where $\Gamma_\Sigma=\Gamma_H+\Gamma_{H^+}$. The results of the calculation of n_2 indicate an appreciable polarity of the bonds between platinum and rhodium on the one hand, and oxygen on the other[138,158,163]. The chemisorption of an ion j on a platinum electrode is characterised by two formal charge-transfer coefficients:

$$n_j'=(\partial\Gamma_H/\partial\Gamma_j)_{\Gamma_{\Sigma,\varphi}} \tag{7a}$$

and

$$n_j''=(\partial\Gamma_{H^+}/\partial\Gamma_j)_{\Gamma_{\Sigma,\varphi}}, \tag{7b}$$

where Γ_j is the Gibbs adsorption of the ion.

VI. THE INFLUENCE OF THE pH OF THE SOLUTION ON THE STRUCTURE OF THE ELECTRODE/SOLUTION INTERFACE

The thermodynamic theory yielded relations between z.t.c.p. and z.f.c.p. on the one hand and the concentration of the neutral salt at a constant pH (and also at a constant concentration of the acid or alkali in solution) on the other[101,123]:

$$(\partial\varphi_r/\partial\mu^{\pm}_{CA})_{Q,\mu_{H^+}}=-(\partial\Gamma_{C^+}/\partial Q)_{\mu^{\pm}_{CA},\mu_{H^+}}-(\partial\Gamma_{A^-}/\partial Q)_{\mu^{+}_{CA},\mu_{H^+}}; \tag{8}$$

$$(\partial\varphi_r/\partial\mu^{\pm}_{CA})_{\Gamma_{H^+},\mu_{H^+}}=-2(\partial\Gamma_{C^+}/\partial\Gamma_{H^+})_{\mu^{\pm}_{CA},\mu_{H^+}}-$$
$$-2(\partial A_H/\partial\mu_{CA})_{\varphi_r,\mu_{H^+}}/(\partial\Gamma_{H^+}/\partial\varphi_r)_{\mu_{H^+},\mu^{\pm}_{CA}}, \tag{9}$$

where $\mu^{\pm}_{CA}$ is the average chemical potential of the salt ions. These expressions can be referred to as the relations for the Esin–Markov coefficient in the case of platinum metals. Owing to the presence of two total charges (Q and Γ_{H^+}), there exist two Esin–Markov coefficients for platinum metals, in contrast to mercury. When a comparison is to be made with a mercury electrode, one should evidently use the quantity $(\partial\varphi_r/\partial\mu^{\pm}_{CA})_{\Gamma_{H^+}\mu_{H^+}}$.

Eqns. (8) and (9) become identical and the same as the relation for mercury when the electrode surface is free from adsorbed hydrogen and oxygen atoms (the double-layer potential range). Direct determinations of the Esin–Markov coefficients in the double-layer region[101] led to the conclusion that they are equal to −1, i.e. that there is no discreteness effect in the adsorption of anions on platinum metals. This phenomenon has been explained by pronounced charge transfer from the anions to the surface of the metal.

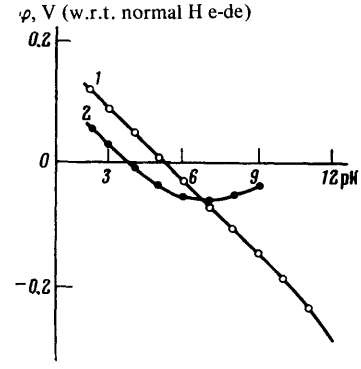

Figure 2. Variation of z.t.c.p. (curve *1*) and z.f.c.p. (curve *2*) with solution pH for a platinised platinum electrode in 0.1 *N* KCl (according to the data of Frumkin et al.[130]).

The variation of z.t.c.p., z.f.c.p., and Γ_{H^+} with solution pH is of special interest, The variation of z.t.c.p. for platinum and rhodium with pH over the entire range of the latter was found directly by the method of potentiometric titration under isoelectric conditions[127-131] (Fig. 2). It was found that at lower pH values, the potential $\varphi_{Q=0}$ shifts in a negative direction by 35–50 mV (depending on the composition of the solution and the nature of the metal) when pH is increased by unity. This relation becomes somewhat more marked at higher pH values and, for example in the case of the rhodium electrode in 0.1 *N* Na_2SO_4 at pH 7–12, the shift of $\varphi_{Q=0}$ amounts to about 58 mV per pH unit. According to the thermodynamic theory, we have for solutions with an excess of the salt[120]

$$(\partial\varphi/\partial\mu_{H^+})_{Q=0}=[1-(\partial\epsilon/\partial A_H)_{\mu_{H^+}}]^{-1}. \tag{10}$$

The observed relations between $\varphi_{Q=0}$ and pH imply that at lower pH values $(\partial\epsilon/\partial A)_{\mu_{H^+}}<0$, i.e. the free charge becomes more positive when φ_r shifts. At pH values in the alkaline region $(\partial\epsilon/\partial A_H)_{\mu_{H^+}}\simeq 0$, which corresponds to the relatively weak dependence of Γ_{H^+} on φ_r in alkaline solutions.

The variation of z.f.c.p. and Γ_{H^+} with pH was first observed by Shlygin et al.[6] Subsequently interest in this problem was aroused by the study of Kheifets and Krasikov[167]. The influence of pH on the z.f.c.p. values for platinum metals has been investigated[109,115,116,168,169]. The most complete data have been obtained by the method of potentiometric titration under isoelectric conditions[130,131]. Fig. 2 illustrates the variation of z.f.c.p. with pH for a platinised platinum electrode in 0.1 M KCl solution. A similar variation of z.f.c.p with pH was also found for platinised platinum and rhodium electrodes in 0.1 N Na_2SO_4. It follows from Fig. 2 that in the pH range 2.3–5 z. f. c. p. shifts with increasing pH towards cathodic values by about 35 mV when the pH is altered by unity. In the pH range 5–9 the shift of z. f. c. p. is small, and at pH > 7 z. f. c. p. begins to shift in the positive direction as the pH is increased. The complex variation of $\varphi_{\Gamma_{H^+}=0}$ with pH is due to the fact that $\varphi_{\Gamma_{H^+}=0}$ shifts from the hydrogen to the double layer region and then to the region where adsorbed oxygen is deposited. The following relation holds for the variation of z.f.c.p. with pH:[106,107,109]

$$(\partial\varphi/\partial\mu_{H^+})_{\Gamma_{H^+}=0} = [1 - (\partial\epsilon/\partial A_H)_{\varphi_r}]^{-1}, \qquad (11)$$

which shows that the shift of z.f.c.p. in the negative direction with increasing pH corresponds to $(\partial\epsilon/\partial A_H)_{\varphi_r} < 0$. When $A_H = 0$, we obtain $(\partial\varphi/\partial\mu_{H^+})_{\Gamma_{H^+}=0}$, and when $(\partial\epsilon/\partial A_H)_{\varphi_r} > 1$, the shift of z.f.c.p. may be in the positive direction. Then pH ~7, $\varphi_{Q=0} = \varphi_{\Gamma_{H^+}=0}$ (Fig. 2). In this case $\varphi_{Q=0}$ and $\varphi_{\Gamma_{H^+}=0}$ correspond to the double layer region of the platinum electrode, i.e. to the region of its ideal polarisability where $Q = \Gamma_{H^+}$.

The results made it possible to plot the variation of z.f.c.p. with A_H and to find its value for $A_H = 0$, i.e. for the platinum surface free from hydrogen and oxygen. It proved to be −0.06 V (relative to the normal hydrogen electrode). Thus z.f.c.p. for the platinum surface free from hydrogen and oxygen is more positive by only 0.2–0.3 V than z.c.p. for mercury. The difference $\varphi^{Pt}_{\epsilon=0} - \varphi^{Hg}_{\epsilon=0}$ is inconsistent with the familiar relation between the electron work function and z.c.p.,[170–172] since the difference between the electron work functions of platinum and mercury is 0.9–1.0 V according to ultrasonic measurements[173]. The problem of the causes of the discrepancy requires further study. Possibly it is associated with the different structures of the adsorbed layers of water on platinum and mercury and with the difference between the structure of platinum crystallites grown in contact with water or platinum subjected to anodic-cathodic activation on the one hand and platinum treated with ultrasound at a high temperature on the other.

Fig. 3 presents the variation of the free surface charge of a platinised platinum electrode with potential in 0.1 M KCl solution at different pH values obtained by the method of potentiometric titration under isoelectric conditions[130]. These data make it possible to put forward the hypothesis of a gradual transition with increasing pH to an electrode surface negatively charged throughout the entire range of φ_r. Such a phenomenon is typical for all platinum metals. Its interpretation is based on allowance for the simultaneous influence of two factors: the shift of the range of potentials in which measurements are made in the negative direction and a more pronounced overlapping of the regions corresponding to the adsorption of hydrogen and oxygen as the pH is increased. Hydrated surface oxide groups are probably weakly acidic and split off hydrogen ions in alkaline media, adsorbing cations. Thus in alkaline solutions there is a transition from the adsorption of cations, caused by the ionisation of the adsorbed hydrogen and decreasing over a range of φ_r values, to the adsorption of cations on the surface of oxide groups, which becomes more marked also over a range of φ_r values.

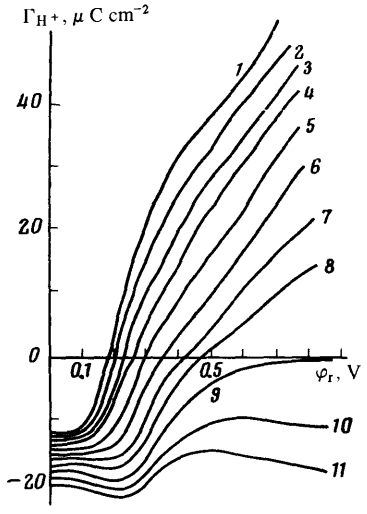

Figure 3. Variation of the free surface charge of a platinised platinum electrode with φ_r in 0.1 N KCl at different pH: 1) 2.3; 2) 3; 3) 4; 4) 5; 5) 6; 6) 7; 7) 8; 8) 9; 9) 10; 10) 11; 11) 12 (according to the data of Frumkin et al.[130]).

The relation between the degrees of adsorption of hydrogen and oxygen ions and atoms leads to the possibility of observing under certain conditions at a constant pH two values of z.f.c.p. corresponding to the reduced and oxidised electrodes. The existence of z.f.c.p. for oxidised platinum followed from the measurements of Balashova and Frumkin[174]. Two values of z.f.c.p., at 0.13 ± 0.02 V and 0.47 V (relative to the normal hydrogen electrode), were found[168] by the radioactive tracer method in a 0.04N Na_2SO_4 solution at pH 6. A similar phenomenon occurs in 0.004N Cs_2SO_4 solution. Two values of z.f.c.p. were observed for iridium in a 1N KI + 0.01N KOH solution[115] (Table 2). Only one value of z.f.c.p. was found for ruthenium[103], in the region corresponding to the adsorption of oxygen, since the z.f.c.p. for the reduced electrode is in the region corresponding to the evolution of molecular hydrogen. Owing to the overlapping of the regions corresponding to the adsorption of hydrogen and oxygen and their involvement in the potential jump at platinum metals, conditions can arise, in principle, over a relatively wide range of potentials where the surface carries almost no free charge (see, for example, curve *9* in Fig. 3).

The rhodium electrode–0.1 M KCl system proved to be particularly convenient for the observation of two values of z.f.c.p. and for the investigation of their characteristics. The results of the determination of the variation of Γ_{H^+} with φ_r for this system by the method of potentiometric titration under isoelectric conditions are

illustrated in Fig. 4. The z.f.c.p. corresponding to oxidised rhodium shifts in the negative direction by 80–140 mV when the pH increases by unity.

At high anodic potentials oxide ions are probably formed with participation of oxygen and the cations and anions of the supporting electrolyte[175–180]. Experiments by the tracer atom method indicate a non-monotonic change with potential in the charge of the metallic component of the ion double layer in this range of polarisations[179,180].

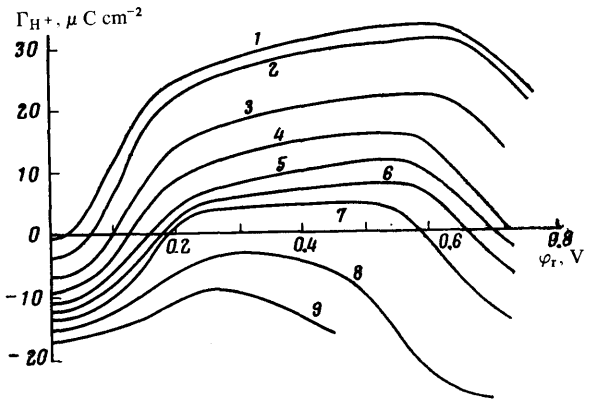

Figure 4. Variation of the free surface charge of a rhodium electrode with φ_r in 0.1 *N* KCl at different pH: 1) 3; 2) 4; 3) 5; 4) 6; 5) 7; 6) 8; 7) 9; 8) 10; 9) 11 (according to the data of R. Notoya's data).

The adsorption of ions is greatly influenced by the inhomogeneity of the surfaces of platinum metals, which has been specially emphasised in a number of publications[20–23]. The inhomogeneity leads to a logarithmic Temkin isotherm for the relation between the adsorption of ions and their concentration in solution and to the Roginskii–Zel'dovich equation for the kinetics of the adsorption of ions[20–23,181–184]. The intrinsic inhomogeneity of the surface of platinum has been demonstrated[185] by differential isotopic methods. Among the interesting conclusions reached in the study of the exchange of ions adsorbed on platinum metals for ions from the solution, the conclusion that a transition state involving both an adsorbed ion and an ion from the solution must be formed in the exchange process[186] is noteworthy.

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Some Problems of Electrochemical Kinetics in the Light of Photoemission Studies

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It is shown on the basis of photoemission data that the electronic work function of a metal in solution is independent of the nature of the metal. The photoemission method for the measurement of the Ψ' potential yields results which agree with calculations based on the Gouy-Chapman theory. Measurements of photocurrents in acid solutions permit the experimental observation and investigation of non-activated electrochemical reactions of atomic hydrogen on various metals.
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INTRODUCTION

The specific features of photoelectron emission at the interface between metals and electrolyte solutions[1], whereby a distinction can be drawn between such emission and photoemission from metals into a vacuum, are associated primarily with the presence of the electrical double layer at the metal–solution interface, and also with the occurrence of homogeneous and heterogeneous reactions in the vicinity of the electrode. These are manifested in a series of general relations typical for the usual electrode processes. Therefore the study of the photoemission of electrons may be regarded as a new approach to the investigation of the fundamental problems of the electrical double layer structure and electrode kinetics. In this connection it is significant that photoemission constitutes the simplest form of electron transition at the interface which is not associated with adsorption and dissociation or formation of chemical bonds and it is therefore particularly convenient for investigations of this kind. Certain results of photoemission studies are discussed below, these are closely related to the fundamental problems of modern theoretical electrochemistry in the formulation and solution of which Frumkin's studies have been of decisive importance.

II. THE ELECTRONIC WORK FUNCTION OF THE METAL IN SOLUTION AND THE NATURE OF THE METAL

The photoemission of electrons from a metal into an electrolyte solution is a threshold phenomenon, like photoemission into a vacuum, the quantitative description of which is based on the concept of the electronic work function of the metal in the given medium. Owing to the presence of the electrical double layer, in which virtually the entire potential jump between the metal and the solution is concentrated, the electronic work function of the metal in solution w_{ms} depends on the electrode potential:

$$w_{ms} = w^0_{ms} + e\varphi, \qquad (1)$$

where w^0_{ms} is the work function of zero potential and e the absolute electronic charge. In photoemission Eqn. (1) is valid provided that the electrical double layer is completely transparent to the emitted electrons[2]. In contrast to emission into an electrolyte, for emission into a vacuum the electronic work function is almost independent of the potential difference applied from the outside (with the exception of special cases in autoelectron emission), since the resulting barrier due to the internal potential difference between the photocathode and anode extends throughout the space between the electrodes and is therefore impermeable to photoelectrons.

For this reason, the concepts of the electronic work function of the metal *in vacuo* and in an electrolyte are not physically equivalent. In the first system the electron work function is understood as the work of transferring the electron from the bulk of the metal into a vacuum to a distance where the Volta potential is constant (this distance is of the order of 10^{-5}–10^{-4} cm).[3] In the general case this work differs from the work of transferring the electron from the metal to infinity *in vacuo* (the electrochemical potential). In the second system the electronic work function is the work of transferring the electron from the metal to the bulk of the solution where there is no double layer field.

Metals at the same electrode potential are characterised by identical electronic work functions in solution, since in this case electron transfer from one metal to another does not require an expenditure of energy. Therefore Eqn. (1) is universal and independent of the nature of the metal.

The quantitative relation between the photocurrent j, on the one hand, and the energy of the light quantum $\hbar\omega$ and the electrode potential, on the other, is described by a 5/2 law[1]:

$$j = A(\hbar\omega - \hbar\omega_0 - e\varphi)^{5/2}, \qquad (2)$$

where $\hbar\omega_0 = w^0_{ms}$ and A is a constant which depends on the nature of the metal. Extrapolation of the experimental $j^{0,4}$–φ photocurrent curve on the basis of Eqn. (2) makes it possible to find the threshold potential φ_0 and hence the electron work function at $\varphi = 0$:

$$w^0_{ms} = \hbar\omega - e\varphi_0.$$

Experimental data obtained for different metals are presented in Fig. 1.[4] The zero-charge potentials of the test metals and hence their electronic work functions *in vacuo*

differ significantly (by up to 0.5 V). On the other hand, the threshold photoemission potentials are the same within the limits of experimental error.

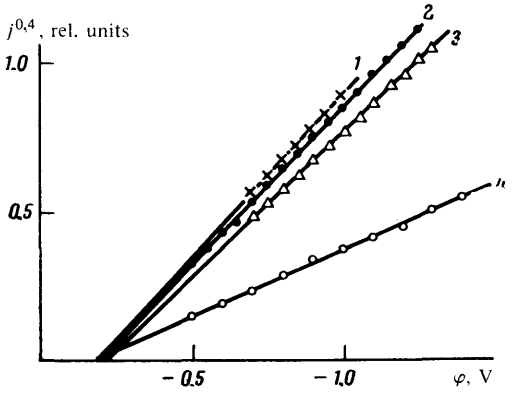

Figure 1. The constancy of the photoemission threshold: 1) indium (0.1 *N* KF); 2) bismuth (0.5 *N* KCl); 3) lead (0.5 *N* Na_2SO_4); 4) mercury (0.5 *N* KF); electron acceptor—O_2; light wavelength —365 nm; the potentials are quoted relative to the saturated calomel electrode throughout.

There exists a universal empirical relation (for aqueous solutions, potential measured relative to saturated calomel electrode) for the electronic work function w_{ms}, which is independent of the nature of the metal which determines φ_0:

$$w_{ms}(\varphi) = 3.45 + e\varphi. \qquad (3)$$

The conclusion that the electronic work function is independent of the nature of the metal agrees with the concepts developed for the first time by Frumkin[5,6], according to which the electronic work function *in vacuo* does not enter in an explicit form into the kinetic slow discharge equation when the potential is referred to a fixed reference electrode.

The constancy of the threshold potential is maintained also when the structure of the electrical double layer is altered (for example, on specific adsorption of various substances, which alter the zero-charge potential), since the double layer remains fairly thin and therefore transparent to the emitted electrons[7].

III. THE "ψ' CORRECTION" IN PHOTOEMISSION AND THE POSSIBILITY OF A DIRECT EXPERIMENTAL DETERMINATION OF THE ψ' POTENTIAL

The kinetics of electrode reactions were considered for the first time in Frumkin's studies[8] in relation to the electrical double layer structure. In the simplest but fairly general case the influence of the double layer on the rate of the electrode reaction is taken into account quantitatively by introducing the ψ' potential into the equation for the slow discharge current. In photoemission the role of the double layer is in many ways similar to its role in electrochemical kinetics. Whereas in concentrated electrolyte solutions the double layer is almost transparent to photoelectrons, in dilute solutions its diffuse component is no longer transparent to such electrons, since its thickness may exceed (for electrolyte concentrations smaller than 0.1 *N*) the de Broglie wavelength of the emitted electrons. In this case the electronic work function changes (relative to the value for the concentrated solution) by an amount $e\psi'$ and the photoemission equation (2) becomes[1]:

$$j = A[\hbar\omega - \hbar\omega_0 - e(\varphi - \Psi')]^{3/2}. \qquad (4)$$

It follows from Eqn. (4) that the rate of photoemission is not influenced by the total φ potential jump, but only by its component $\varphi - \psi'$. The complete analogy with the influence of the ψ' potential on the activation energy for the discharge of the species in the outer Helmholtz plane of the electrical double layer is striking.

The possibility, in principle, of an experimental determination of the ψ' potential follows from a comparison of the emission photocurrents in dilute [Eqn. (4)] and concentrated [Eqn. (2)] solutions. †

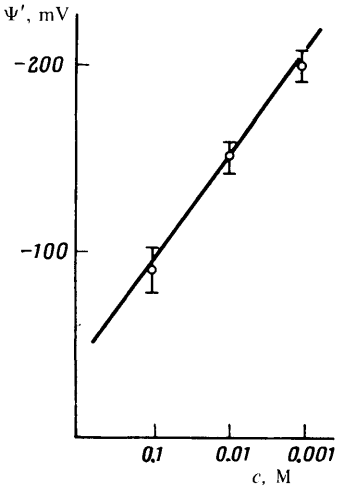

Figure 2. Variation of the ψ' potential with the concentration of the electrolyte (HCl); mercury electrode, -1.1 V; continuous straight line —calculation based on the Gouy–Chapman theory.

The photocurrents for mercury and lead electrodes have been measured[9] in HCl solutions at different concentrations (from 0.001 to 1 *N*) and negative potentials where $\psi' < 0$. The ψ' potentials found from the shift of the $j^{0,4} - \varphi$ curves in dilute acid solutions along the potential axis relative to the curve in 1 M HCl are presented in Fig. 2 as a function

† In general, difficulties arise in such measurements; these are associated with the influence of the structure of the double layer not only on the emission step itself, which is described by Eqns. (2) and (4), but also on the processes accompanying emission. These processes are mainly migration of hydrated electrons in the field of the diffuse layer. To eliminate undesirable effects of this kind, which complicate the determination of the ψ' potential, it is necessary to create conditions where hydrated electrons hardly return to the electrode and therefore the influence of the structure of the double layer reduces merely to a change in the emission current itself. In the measurements described below this condition was fulfilled.

of the logarithm of the concentration of the electrolyte. The continuous straight line was calculated on the basis of the Gouy–Chapman theory. The quantitative agreement between the experimental and theoretical data is of fundamental importance, since the photoemission method for the determination of the ψ' potential and the traditional differential capacitance method are based on completely different physical approaches. It must be emphasised that in the Gouy–Chapman theory one considers the ψ' potential averaged over a plane parallel to the electrode surface and not the local ψ' potential which can be determined, in principle, from kinetic measurements. By virtue of the delocalisation of the emitted electron in this plane, the averaged ψ' potential is also measured by the photoemission method. Therefore the above comparison of the theory with experiment is physically justified.

IV. THE OBSERVATION AND INVESTIGATION OF ELECTRODE REACTIONS WITHOUT ACTIVATION ENERGY

Electrode reactions differ from the usual chemical reactions specifically by the fact that their activation energies increase linearly with electrode potential. On the basis of the Brønsted relation, Frumkin et al.[10] concluded that at high overvoltages the activation energy for the electrode process can become zero and the rate of reaction can cease to depend on the potential. Such non-activated electrode reactions could not be detected until recently by the usual electrochemical methods because the direct measurement of the limiting currents for non-activated discharge was precluded by diffusion-dependent restrictions, which inevitably arose. Only recently was a system discovered[11] in which the supply of the reactant to the surface did not constitute the rate-determining step and the measured limiting current could be treated as the current of a process without activation energy ‡.

Electrode reactions without activation energy were observed for the first time (although not by direct measurement of the limiting current) in a study of the photoemission of electrons from mercury in acid solutions[13]. As a result of the capture of hydrated electrons by the hydronium ions in the layer of solution adjoining the electrode, hydrogen atoms are formed and then removed from the electrode surface via two electrochemical reactions:

$$H + H_2O\,(H_3O^+) + e^- \rightarrow H_2 + OH^-\,(H_2O); \quad (5)$$

$$H + H_2O \rightarrow H_3O^+ + e^-. \quad (6)$$

The measurement of the photocurrent in such systems and in systems where there is no oxidation of atomic oxygen makes it possible to determine the ratio of the currents consumed in the oxidation and reduction of hydrogen atoms. Analysis of the kinetic scheme showed that this ratio is $(2j_0 - j)j$, where $2j_0$ is the photocurrent in the absence of the oxidation of hydrogen and j is the measured photocurrent. The variation of $(2j_0 - j)/j$ with φ is described by the equation[13]

$$\varphi = \frac{2.3\,RT}{(\alpha + \beta)\,F}\left(\lg\frac{2j_0 - j}{j} + \text{const}\right), \quad (7)$$

‡ Krishtalik's observation[12] of barrier-free hydrogen ion discharge processes served as direct evidence for the occurrence of non-activated ionisation of hydrogen on mercury.

from which it is possible to determine the sum of the transfer coefficients $(\alpha + \beta)$ for the two coupled reactions (5) and (6).

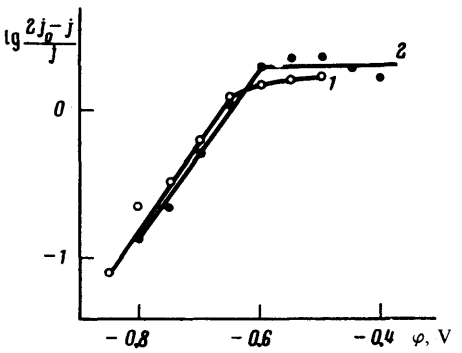

Figure 3. Determination of the transfer coefficients for the reactions of atomic hydrogen on bismuth by Eqn. (7): *1*) 0.5 *N* KBr + 0.003 *N* HCl; *2*) 0.5 *N* KCl + 0.06 *N* HCl.

As an example, Fig. 3 illustrates the graphical treatment in terms of Eqn. (7) of experimental data obtained for a bismuth electrode[4]. At potentials more positive than -0.6 V the ratio of the atomic hydrogen oxidation and reduction currents is independent of φ and, when $\varphi < -0.6$ V, the ratio decreases with the potential. Accordingly, $\alpha + \beta = 0$ in the region of positive potentials and $\alpha + \beta = 0.4$ in the region of negative potentials. The sum of the transfer coefficients being equal to zero is equivalent to each being zero. Thus reactions (5) and (6) both proceed without activation energy when $\varphi > -0.6$ V. The electrochemical desorption reaction (5), being a cathodic reaction, remains without activation energy (i.e. $\alpha = 0$) also at negative potentials when $\alpha + \beta = 0.4$. Hence it follows immediately that the transfer coefficient for the hydrogen ionisation reaction $\beta = 0.4$. This value agrees with the results of direct measurements of the rate of discharge of the H_3O^+ ion on bismuth[14], for which the transfer coefficient $1-\beta = 0.6$; this also demonstrates the overall self-consistency of the process mechanism described. The electrochemical desorption reaction (5) on bismuth proceeds mainly with participation of water molecules, in agreement with the hypothesis that the process mechanism involves zero activation energy[15].

Reactions with zero activation energy involving atomic hydrogen have also been observed on mercury[13] and antimony[16]. The kinetics of these processes are sensitive to the adsorption on the electrode of various substances which alter the structure of the double layer and may be formally interpreted[4] on the basis of Frumkin's theory of the ψ' effect.

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Electrochemical Oxidation of Organic Compounds on Anodes Consisting of Certain Transition Metal Oxides

M.Ya.Fioshin and I.A.Avrutskaya

The mechanism and kinetics of the electrochemical oxidation of organic compounds on nickel, cobalt, copper, and silver anodes at potentials corresponding to the formation of the higher oxides of these metals are discussed. The problems of the practical use of the electrodes in the electrosynthesis of organic compounds are examined. The feasibility of different versions of electrosynthetic processes with participation of the higher oxides, regenerated electrochemically, is demonstrated for the nickel oxide electrode.
The bibliography includes 44 references.

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I. INTRODUCTION

Electrochemical oxidation reactions of organic compounds on certain transition metal electrodes coated by oxides have been attracting attention in recent years. The studies using these electrodes have been carried out both from the theoretical standpoint in order to investigate the kinetics and mechanism of the oxidation and from the practical standpoint for the assessment of the possibility of using oxide electrodes in the electrosynthesis of organic compounds. Alcohols[1-3], among which di-*O*-isopropylidene-L-sorbose may also be included[4-7], and amines[3] have been oxidised on a nickel oxide electrode, alcohols and amines[8] on a cobalt oxide electrode, amines[9,10] on silver(II) oxides, and alcohols and amines[11] on copper(III) oxides.

II. KINETICS AND MECHANISM OF THE PROCESSES ON ANODES CONSISTING OF TRANSITION METAL OXIDES

The nature of the phenomena occurring on the surface of anodes consisting of a number of transition metal oxides has not yet been completely elucidated. This is why certain views put forward in the literature are contradictory and serve as a basis for further discussion.

The determination of the complete picture of the processes occurring on these electrodes is apparently precluded by the virtual lack of data on the sorption of organic compounds involved in the oxidation reactions, while adsorption phenomena must be taken into account in seeking new procedures for organic electrosynthesis[12].

It has been shown[11] that the mechanisms of the oxidation of alcohols and amines on nickel, cobalt, copper, and silver anodes coated by the oxides are similar and do not involve simple electron transfer, as happens, for example, in the oxidation of amines on graphite.

Potentiodynamic measurements established that the first oxidation stage involves the electrochemical formation of the higher metal oxide and that the entire mechanism can be represented schematically as follows:

$$OH^- + \text{lower oxide} \overset{\text{fast}}{\rightleftharpoons} \text{higher oxide} + H_2O + e; \quad (1)$$

$$(\text{organic substrate})_{soln} \overset{\text{on higher oxide}}{\rightleftharpoons} (\text{organic substrate})_{ads}; \quad (2)$$

$$\text{higher oxide} + (\text{organic substrate})_{ads} \rightarrow \text{lower oxide} + \text{intermediate radical (rate-determining stage)}; \quad (3)$$

$$\text{intermediate radical} - (n-1)e \rightarrow \text{product} \quad \text{or} \quad (4)$$

$$\text{intermediate radical} + (n-1)\,\text{higher oxide} - (n-1)\,\text{lower oxide} + \text{product} \quad (5)$$

here n is the number of electrons involved in the reaction.

For thin oxide layers (particularly on nickel), the equilibrium corresponding to reaction (1) is established rapidly[13], while for thicker layers the diffusion of electroactive species in the film becomes rate-determining[14]. However, according to other data[15] the existence in the oxidation of organic compounds of an equilibrium between the lower and higher nickel oxides, involving nickel hydroxide in the case of thin layers, appears to be doubtful.

Many experimental data[11] support the idea that the organic compounds are oxidised in the adsorbed state on the higher oxide in accordance with reaction (2), although adsorption has not been the subject of a special study and the weak adsorbability of organic substances on iron-group and silver-group metals under analogous conditions has been merely mentioned[16].

The next stage [stage (3)], involving the interaction of the adsorbed organic compound with the higher oxide, was studied in greatest detail, particularly for the nickel oxide electrode. The oxidation of various substances on each electrode proceeds at the same potentials, corresponding to the formation of the higher oxides of the given metal[11]. The mechanism involving a chemical interaction of the organic substance with the higher oxide is indicated by the absence of a dependence of the oxidation current on the potential at low currents and by the dependence of the limiting rate of the electrochemical reaction on the rate of rotation of the disc electrode. Furthermore, a cathodic current is not revealed by the cyclic voltage–current curves for the oxidation process on transition metal oxide anodes in the presence of organic compounds at low rates of application of the potential, and high activation energies for the electrode process have been noted.

To confirm the hypothesis that a chemical reaction mechanism is possible, one can employ data for the chemical oxidation of certain organic compounds by the higher oxides of the same metals. Thus in the oxidation

of alcohols[17] and amines[18] by higher nickel oxides the same products are formed as in the anodic oxidation.

The chemical interaction with the higher oxide probably proceeds in the solid phase and is not associated with the transfer of the metal to the solution, since corrosion of the anode is not observed in the oxidation process. To estimate the rate of chemical interaction of the organic substance with the higher oxide, a study has been made (particularly for nickel) of the time variation of the potential of a non-polarised nickel oxide electrode in the course of its joint reduction by the cathodic current and the compound being oxidised[19]. These results established that the rate of reaction is proportional to the concentration of the organic compound and the amount of the higher oxide on the electrode surface. The calculated chemical oxidation rate constants for certain alcohols are listed in Table 1.

Table 1. The rate constants k for the oxidation of various alcohols on a nickel oxide electrode.

Alcohol	k, mole^{-1} s^{-1}	Alcohol	k, mole^{-1} s^{-1}
Methyl	0.04	Benzyl	0.4
Ethyl	0.06	Furyl	0.8

However, data obtained later by the same authors using the potentiodynamic method[15] conflict, in their view, with the earlier conclusion that the rate of oxidation is proportional to the amount of higher oxide on the electrode surface. According to these data[15], the rate of reaction depends to a considerable degree on the previous history of the electrode. In particular, the rate is greatly reduced on the surface of a nickel oxide electrode which had been subjected to a preliminary oxidation. An increase of the amount of higher oxide of the type NiOOH on the electrode surface has an inhibiting effect on the oxidation reaction. The authors to not rule out the possibility of a direct interaction between the higher nickel oxide and the organic compound but the rate of the reaction must be lower than the rate of oxidation on the fully oxidised surface at potentials which are insufficient for the electrochemical reduction of the oxide layer.

On the other hand, according to other results[11] direct electron transfer in the rate-determining stage is unlikely, since secondary amines are oxidised more slowly than primary amines and tertiary amines are not oxidised at an appreciable rate. This is also confirmed by the occurrence of a kinetic isotope effect in the oxidation of normal and deuterated methanol ($k_{CH_3OH}/k_{CD_3OH} = 7.0$). A similar kinetic isotope effect was observed also in the chemical oxidation of diphenylmethanol by higher nickel oxides ($k_{(C_6H_5)_2CHOH}/k_{(C_6H_5)_2CDOH} = 7.4$).[20]

These results suggest that the rate-determining stage is the abstraction of a hydrogen atom from the molecule of the compound being oxidised with formation of free-radical species [reaction (3)], occurring in the interaction with higher metal oxides. In the chemical oxidation of a series of substances by higher nickel oxides the formation of radicals was confirmed by ESR.[20] A study of the electrochemical oxidation of alcohols to acids on a nickel oxide electrode also established that the rate-limiting stage is the oxidation of the alcohol to the aldehyde[21].

The mechanism of the oxidation of certain organic compounds on a nickel electrode may change depending on the potential, this being related to the degree of oxidation of the electrode surface. At negative potentials the reaction proceeds as a result of direct electron transfer to the smooth nickel electrode or via a dissociative adsorption mechanism[22], while at more positive potentials the oxidation mechanism includes a chemical reaction between the higher nickel oxide and hydrazine[23].

All the above remarks concerning the mechanism of the oxidation of organic compounds on oxide electrodes make it possible to classify the higher oxides of these metals as heterogeneous catalytic transferring agents.

III. ELECTROSYNTHESIS OF ORGANIC COMPOUNDS ON CERTAIN TRANSITION METAL OXIDE ELECTRODES

The data concerning the use of certain transition metal oxide electrodes in the electrosynthesis of organic compounds are few. Table 2 presents comparative results for the oxidation of alcohols and amines on electrodes coated by oxides[11].

Table 2. Current yields of the products of the oxidation of alcohols and amines on anodes coated by oxides.

Starting material	Reaction products	Current yield, %		
		nickel (0.55 V)	silver (0.75 V)	copper (0.7 V)
n-Propylamine	Propionitrile	84	83	85
	Propionaldehyde	11	2	2
n-Butylamine	Butyronitrile	85	85	–
	Butyraldehyde	6	2	–
Isopropylamine	Acetone	80	70	85
Diethylamine	Acetonitrile	46	27	30
	Acetyldehyde	3	3	5
	Acetic acid	36	29	40
Ethanol	Acetic acid	98	–	96
1-Propanol	Propionic acid	95	–	–
2-Propanol	Acetone	90	–	9

The oxidation of alcohols to the corresponding acids in an alkaline medium proceeds on these electrodes with a higher selectivity than in electrolysis in acid solutions on platinum and lead dioxide anodes and makes it possible to avoid esterification reactions, which complicate the process in an acid medium.

Among the electrodes considered, the nickel oxide electrode has been most widely used in the electrosynthesis of organic compounds. It is noteworthy that the specificity of the oxidation on oxide electrodes has also been reflected in the practical application of processes involving higher nickel oxides. There is a fairly wide variety of different ways in which electrosynthetic processes involving higher nickel oxides, regenerated electrochemically in the course of the oxidation, can be carried out. The electrochemical oxidation is performed at an electrode obtained by depositing nickel(II) hydroxide on an inert current-conducting base with subsequent formation of the higher oxide on anodic polarisation[1]. The positive plates of iron–nickel and cadmium–nickel accumulators have also been used as the anodes[5,24–27]. The nickel

oxides may be present in solution as a suspension. Solutions of an alkali[24,25,28,29] or an alkali metal halide[30-39] are used as the electrolyte. In electrolysis in a solution of alkali the higher oxide is regenerated during the transient contact between the solid particle and the current lead. During electrolysis, the current lead is coated by nickel oxides and, as shown below, acquires the properties of a nickel oxide electrode. When the electrolyte is a halide solution, the higher oxide is regenerated both electrochemically and, as in chemical oxidation[17,40], by the interaction with the hypohalite. The oxidation of di-*O*-isopropylidene-L-sorbose (DAS) to di-*O*-isopropylidene-2-oxo-L-gulonic acid (DOGA)—the intermediate in the synthesis of ascorbic acid—has been investigated in detail in the presence of bromides. Under these conditions, the oxidation mechanism can be represented schematically as follows[35]:

$$2\,Br^- - 2e \rightarrow Br_2 \text{ (on the anode)};$$
$$Ni(OH)_2 - e \rightarrow NiOOH + H^+ \text{ (on the anode)};$$
$$Br_2 + 2\,OH^- \rightarrow BrO^- + Br^- + H_2O;$$
$$2\,Ni(OH)_2 + NaBrO \rightarrow 2\,NiOOH + NaBr + H_2O;$$
$$C_{11}H_{17}O_5CH_2OH + 4\,NiOOH + H_2O \rightarrow C_{11}H_{17}O_5COOH + 4Ni(OH)_2.$$

Table 3. The influence of the anode material on the electrochemical oxidation of DAS (0.289 M DAS, 3% NaOH. Q = 1 Ah/g DAS, t = 60°C).

Anode material	Current density, A dm^{-2}	Amount of DAS in soln., g: init.	Amount of DAS in soln., g: residual	Electrode potential, V (w.r.t. normal H e-de)	$NiCl_2 \cdot 6H_2O$, N	Yield of DOGA, %: material: w.r.t. init DAS	Yield of DOGA, %: material: w.r.t. DAS which has reacted	Yield of DOGA, %: material: current	Average current yield of oxygen, %
Nickel foil	5	10.5	1.28	0.9—1.2	0.17	69.0	78.7	30.4	—
	5	9.5	9.5	1.06	—	0	0	0	98
Porous nickel	5	9.7	0.1	0.86—1.0	0.17	84.3	85.0	34.6	—
	5	9.2	6.8	0.7	—	traces		—	85
Nickel oxide*	5	9.7	0.6	—	0.042	91.0	96.0	37.0	—
	5	9.8	1.3	0.7—0.8	—	66.8	77.2	27.6	10—70
Nickel oxide**	5	9.7	0.2	0.72	0.042	96.5	98.5	39.8	—
	5	9.43	0.2	0.67	—	90.2	92.0	35.8	20—98
Nickel oxide*** (lamellar)	30	19.0	10.8	—	—	42.0	98.3	16.4	—
Stainless steel (1Kh13N9T)	5	9.5	0.14	1.28	0.17	87.0	88.0	34.9	—
	5	9.3	8.3	0.94	—	0	0	0	94
Electrode graphite	5	19.7	0.13	1.4	0.17	87.5	88.0	35.5	—
	5	10.0	9.1	—	—	0	0	0	—
Platinum	5	9.7	3.7	1.14	0.17	54.6	88.0	22.4	—
	5	9.5	9.1	1.1	—	0	0	0	95
Lead dioxide	5	12.0	—	—	—	0	0	0	95
Manganese dioxide (thermal)	30	10.1	9.2	1.14	—	0	0	0	95
Cobalt oxide (electrolytic)	30	9.9	9.6	—	—	0	0	0	100
Cobalt oxide (thermal)	30	9.9	8.9	1.06	—	0	0	0	95
Ruthenium oxide (thermal)	5	10.1	10.0	1.25	—	0	0	0	100

* Obtained by a single impregnation of porous nickel initially in nickel chloride solution and then in alkali with subsequent anodic polarisation.
** Factory-made foil electrode.
*** c_{DAS} = 0.58 M.

Higher nickel oxides can be used as chemical oxidants with subsequent electrochemical regeneration in a separate apparatus[41]. Isopentyl alcohol was oxidised in this way to isovaleric acid in 80% yield. The nickel oxide electrode has been most widely used in the electrochemical oxidation of alcohols to the corresponding acids in an alkaline medium, the results obtained in the electrochemical oxidation of DAS being of greatest practical importance.

The electrochemical oxidation of DAS in an alkaline medium has many advantages compared with halide solutions from the standpoint of the yield of the product, the efficiency of the process, and also its cost. Therefore the fundamental characteristics of the electrochemical oxidation of DAS with participation of nickel oxides will be examined only for alkaline solutions. The influence of the electrode material on the electrochemical oxidation of DAS in an alkaline medium has been investigated[25]. The results are presented in Table 3 and in Fig. 1.

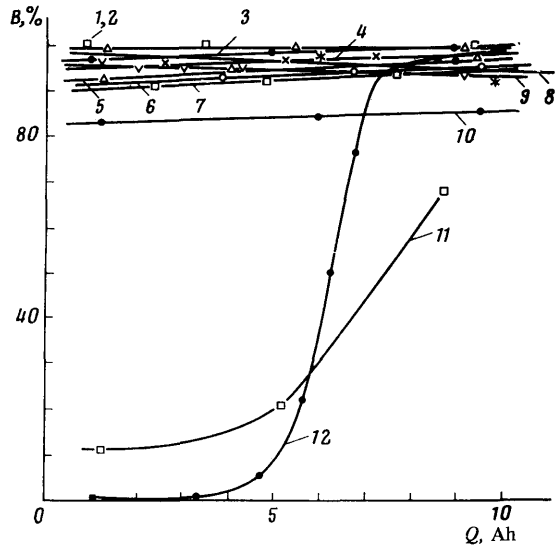

Figure 1. Variation of the current yield of oxygen (B) with the amount of electricity passed through the system in the electrochemical oxidation of DAS on different electrodes: 1) cobalt oxide (electrolytic); 2) ruthenium oxide; 3) nickel; 4) platinum (purified DAS); 5) platinum (technical DAS); 6) cobalt oxide (thermal); 7) stainless steel; 8) lead dioxide; 9) manganese dioxide; 10) porous nickel; 11) nickel oxide (obtained under laboratory conditions); 12) nickel oxide (factory made foil electrode); c_{DAS} = 0.29 M; c_{NaOH} = 3%; t = 60°C; Q = 1 Ah/g DAS.

The current yield of oxygen on nickel, manganese dioxide, lead dioxide, platinum, and stainless steel anodes and also on cobalt oxide and ruthenium oxide electrodes is constant and close to 100%. Accordingly, the consumption of DAS on these electrodes is low (Table 3) and DOGA is not formed.

The electrode potentials at which DAS is oxidised with a low efficiency vary in the range 0.95–1.15 V and there is no definite relation between the electrode potential, the consumption of DAS, and the fraction of the current consumed in its oxidation.

The current yield of oxygen on a porous nickel electrode is 83–84%. DAS is then consumed to an appreciable extent and a small amount of DOGA is formed. A different behaviour has been observed on two nickel oxide electrodes. A considerable proportion of the current was initially consumed in the oxidation of DAS and then, with decrease of its concentration, the current yield of oxygen

rose and reached 100% on an industrial specimen containing a large amount of active mass per unit surface of the electrode. On the second specimen, the fraction of the current consumed in the evolution of oxygen was somewhat higher throughout the experiment and, for the same amount of electricity consumed, the reaction did not reach completion and DAS which failed to react remained. The main oxidation product on nickel oxide electrodes is DOGA, formed in a material yield exceeding 90%. The lower yield of DOGA and the larger amount of DAS which did not react on the lamellar nickel oxide electrode can probably be explained by the poor contact between the solution and the active mass and the consequent decrease of the rate of the chemical interaction.

Comparison of the data for the oxidation of DAS on a smooth nickel electrode, a porous nickel electrode, and three specimens of nickel oxide electrodes makes it evident that the rate of oxidation of DAS increases with increase of the amount of the active mass of the oxides per unit surface of the electrode.

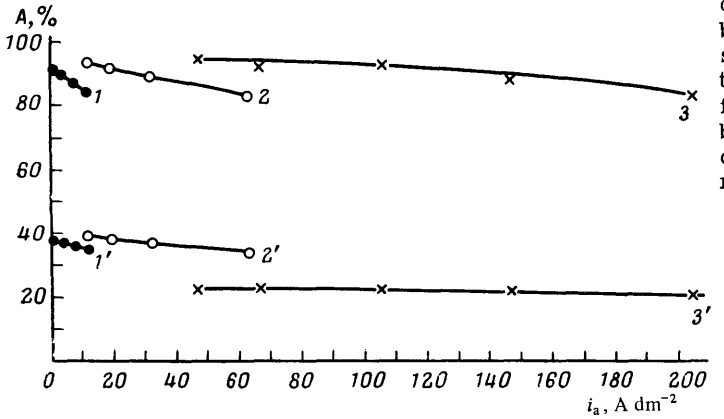

Figure 2. Variation of the yield of DOGA (A) with current density; 0.22 M DAS; 2% NaOH; t = 55°C; Q = 1 Ah/g DAS: 1) and 1′) the material and current yields for coaxially arranged electrodes separated by a distance of 5 mm; 2) and 2′) the material and current yields for horizontally arranged electrodes separated by a distance of 32 mm. 0.4 M DAS; 2.4% NaOH; t = 59°C; Q = 1.72 Ah/g DAS: 3) and 3′) the material and current yields for a vertical arrangement of the electrodes separated by a distance of 25 mm.

The addition of variable-valence metal salts [such as iron(III), cobalt(II), and manganese(II) salts] does not affect the electrochemical oxidation of DAS. The introduction of nickel salts into the solution promotes the formation of DOGA on electrode materials such as smooth nickel, stainless steel, and graphite, on which DOGA could not be obtained in the absence of an additive. The addition of nickel salts increases the yield of DOGA also on nickel oxide electrodes and their effect is more marked on an electrode with a small amount of active mass per unit surface. During electrolysis in the presence of nickel salts, porous electrodes made of different materials become coated by nickel oxides. The presence of nickel compounds on the surface of graphite and in its pores is confirmed by the fact that DOGA is formed even in the absence of an additive on an electrode which had been used beforehand in the presence of nickel salts. In contrast to graphite, the steel electrode remains inactive in subsequent experiments.

The electrosynthesis of DOGA in an alkaline medium on graphite anodes at a current density of 2.4 A dm^{-2} in the presence of dispersed nickel oxides is carried out on an industrial scale using a continuous process[29]. It can be greatly intensified by increasing the current density to 12–15 A dm^{-2}.

It is noteworthy that one of the advantages of the use of nickel oxide electrodes in the electrosynthesis of DOGA is the high rate of the process. Fig. 2 illustrates the influence of current density on the yield of DOGA for different relative positions of the electrodes[5]. When the distance between the electrodes is small, the yield of the product decreases sharply with increase of current density. For a horizontal arrangement of the electrodes and a large distance between them, it is possible to extend greatly the range of current densities without a significant reduction of the material yield of DOGA. At a constant current density the yield depends appreciably on the distance between the electrodes, which can probably be explained by the influence of factors such as the stirring of the electrolyte in the space between the electrodes, the access of the electrolyte to this space, and the filling of the system with gas. For small distances between the electrodes and high current densities, the decisive factor is the filling of the system with gas, which reduces the volume of the reacting solution.

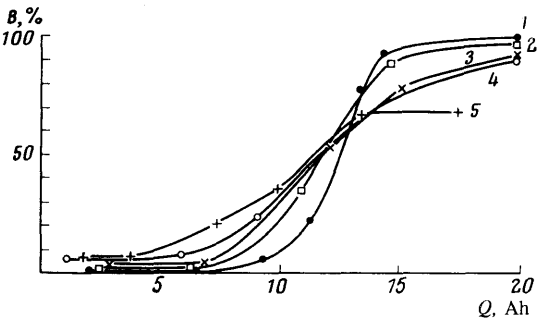

Figure 3. Variation of the current yield of oxygen (B) with the amount of electricity passed through the system at different current densities (Ah dm^{-2}): 1) 5; 2) 10; 3) 21; 4) 29; 5) 50; c_{DAS} = 0.58 M; c_{NaOH} = 3%; t = 60°C.

The optimal conditions for the electrosynthesis of DOGA were established by the simplex design method at a constant current density of 50 A dm^{-2}; then the possibility of carrying out the process at higher current densities was studied under the same conditions. An increase of current density to 100 A dm^{-2} in solutions with high DAS concentrations does not affect appreciably the yield of DOGA (Fig. 2). At higher current densities and a given concentration of alkali the yield falls and the electrode breaks up. The latter is probably associated with the

high rate of the process as a result of which the layer of electrolyte adjoining the anode surface is acidified by the DOGA formed. The change in current density leads to a redistribution of the relative amounts of the current consumed in the electrochemical oxidation of DAS and in the evolution of oxygen (Fig. 3).[24] With decrease of current density, the fraction of the current consumed in the evolution of oxygen falls and the duration of electrolysis increases, which should evidently favour the chemical interaction between DAS and the higher oxides.

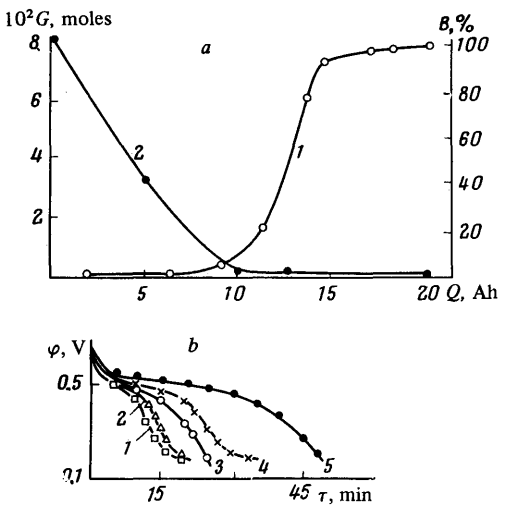

Figure 4. *a*) Variation of the current yield of oxygen (*B*) (curve *1*) and of the amount (*G*) of DAS which failed to react (curve *2*) with the amount of electricity passed through the system; c_{DAS} = 0.58 M; c_{NaOH} = 3%; t = 60°C; i_a = 5 A dm^{-2}; *b*) variation of the potential of a non-polarised nickel oxide electrode with time in 3% NaOH solution at 60°C and different DAS concentrations (M); 1) 0.58; 2) 0.46; 3) 0.35; 4) 0.23; 5) 0.12.

Table 4. The influence of Fe^{3+} ions on the yield of DOGA (c_{DAS} = 0.58 M, c_{NaOH} = 2%, t = 59°C, Q = 1 Ah/g DAS, D_a = 32 A dm^{-2}, $c_{Fe^{3+}}$ = 0.007 M).

No. of expt.	1	2	3	4
Material yield of DOGA, %	91.8	91.6	83.3	81.6
Current yield of DOGA, %	35.8	35.6	32.2	31.6

It is noteworthy that, in the study of the influence of factors such as the concentration of DAS (Fig. 4) and temperature (Fig. 5) on the rate of the process, a correspondence was noted between the changes in the rates of anodic oxidation and chemical interaction. As in an earlier investigation[20], the latter was estimated from the time variation of the potential of a non-polarised nickel oxide electrode discharged in the presence of DAS. Thus the rate of the anodic oxidation of DAS increases with increase of its concentration, the amount of oxides per unit electrode surface, and temperature, and there is a parallel variation of the rate of the chemical interaction of the organic substance with nickel oxides, which may serve as indirect confirmation of their involvement in the oxidation of DAS in the electrolysis, in conformity with the mechanism proposed by Fleischmann et al.[11]

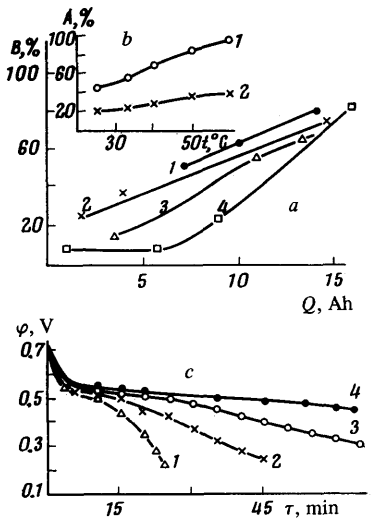

Figure 5. *a*) Variation of the current yield of oxygen (*B*) with the amount of electricity passed through the system at different temperatures (°C): 1) 20; 2) 30; 3) 40; 4) 60; *b*) temperature variation of the material yield of DOGA (*A*) with respect to the DAS introduced (curve *1*) and of the current yield (curve *2*); c_{DAS} = 0.58 M; c_{NaOH} = 3%; i_a = 29 A dm^{-2}; *c*) time variation of the potential of a non-polarised nickel oxide electrode in 3% sodium hydroxide solution at a DAS concentration of 0.35 M and different temperatures (°C): 1) 60; 2) 50; 3) 40; 4) 20.

The extensive experience gained in the use of nickel oxide electrodes in alkaline accumulators has shown that their discharge characteristics are fairly sensitive to inorganic admixtures[42]. The problem of the stability of the active properties of the nickel oxide electrode has also been studied in the electrosynthesis of organic compounds[43]. When the nickel oxide electrode had been used for a comparatively long time, no change in its activity was observed in solutions of purified DAS. Since purification of DAS complicates the technological process and involves loss of product, a study was made of the behaviour of foil and metalloceramic electrodes in the electrochemical oxidation of technical DAS. In contrast to the series of experiments with the purified product, the material yield of DOGA relative to the DAS introduced gradually fell, amounting to 64% on the metalloceramic electrode after the consumption of 2.12×10^3 Ah dm^{-2}, while at the beginning of the series it was 98%. There was a corresponding decrease also of the current yield.

The foil electrode, which contains a smaller amount of active mass per unit geometrical surface of the electrode, loses its activity more rapidly than the metalloceramic electrode. The loss of electrode activity consists in a decrease of the fraction of the current consumed in the electrochemical oxidation of DAS and in an increase of the current yield of oxygen. It has been established that the active properties of the electrode are influenced by inorganic admixtures. Table 4 shows how the yield of DOGA falls gradually under the influence of Fe^{3+} ions.

A similar effect is produced by Ca^{2+} ions. The latter also retard the chemical interaction of DAS and aliphatic alcohols with nickel oxides, which indicates a correspon dence between the rates of the chemical and anodic processes.

The causes of the change in the activity of the nickel oxide electrode are probably analogous to those noted when similar electrodes are used in current sources, their behaviour being determined by the kinetics of the electrochemical oxidation and of the reduction of solid oxides[44], but at much lower current densities.

Different ways of activating nickel oxide electrodes have been investigated. A partial and brief increase of electrode activity occurs after alternate preliminary cathodic and anodic polarisation in a solution of alkali. It is possible to maintain the active properties of the nickel oxide electrode during the electrochemical oxidation of technical DAS by the periodic introduction into the solution of nickel ions (0.01 M), which renews the electrode surface. However, as the electrode continues to be used, the maximum yields are 90–92% after the consumption of $(5.9–6.5) \times 10^3$ Ah dm^{-2} even in the presence of nickel ions, which is somewhat less compared with the results obtained in the absence of additives in the first experiments.

When the electrochemical oxidation of technical DAS on a nickel oxide electrode was carried out with continuous injection of nickel ions (0.004 M), the yield of DOGA remained stable throughout the tests (5.9×10^3 Ah dm^{-2}).

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The Mechanism of the Excitability of Biological Membranes

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The phenomenology of the excitation of a cell membrane is described. It is shown that, in the adsorption inhibition of a mobile transferring agent, the descending branch of the voltage-current characteristic can be obtained. The Hodgkin-Huxley model is interpreted in terms of ionic channels and the statistical properties of such a system are examined. In particular, the spectrum of the electrical fluctuations of potassium channels is analysed. Experiments in which "gating currents" were measured are briefly described and interpreted in terms of the cooperative dipole model.
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I. INTRODUCTION

The phenomenology of the electrical phenomena occurring on excitable cell membranes can be described in detail by the Hodgkin–Huxley empirical equations[1]. Until recently the attempts to create physically consistent models outside the framework of a formal description have been speculative, since a suitable experimental basis was lacking. Nevertheless the endeavour to achieve some kind of physical model is quite justified. Strictly speaking, Hodgkin and Huxley themselves indicated, although not without reservations, one of the simplest possible interpretations of the formal scheme. Studies in recent years on the selectivity and permeability of ionic channels[2,3], experimental and theoretical investigations of the electrical noise spectra of membranes[4-7], and finally brilliant experiments in which measurements were made of the so called "gating currents"[8-11] altered the situation radically. On the one hand, a need arose for certain modifications to the formal Hodgkin–Huxley scheme and on the other a basis appeared for the development of a physical model of excitability. This paper is devoted to a brief analysis of the present state of the problem of excitability.

II. PHENOMENOLOGY OF THE EXCITATION PROCESS

Here we shall describe only briefly the well known model of the squid axon and shall note certain details which we believe to be important. According to the Hodgkin–Huxley model, the membrane potential satisfies the following equation in the process of three-dimensional homogeneous excitation:

$$C\frac{d\varphi}{dt} = -I. \tag{1}$$

The significance of this equation is that the membrane is regarded as a condenser with a capacitance $C \simeq 1\ \mu F\ cm^{-2}$. The ionic current I is formulated as the sum of three currents—the sodium, potassium, and leakage currents:

$$I = I_{Na^+} + I_{K^+} + I_L. \tag{2}$$

In its turn each current is regarded as the current generated by a battery with a constant e.m.f. and a variable resistance (apart from the leakage resistance):

$$I_{Na^+} = g_{Na^+}(\varphi - \varphi_{Na^+}); \tag{3}$$

$$I_{K^+} = g_{K^+}(\varphi - \varphi_{K^+}); \tag{4}$$

$$I_L = g_L(\varphi - \varphi_L);\ g_L \approx 3 \cdot 10^{-4}\ \Omega^{-1}\ cm^{-2}. \tag{5}$$

Each of the three e.m.f.'s (φ_{Na^+}, φ_{K^+}, and φ_L) is assumed to be known and determined by the differences between the concentrations of the corresponding ions in accordance with the Nernst formula. Under physiological conditions, these quantities are $\varphi_{Na^+} = +115$ mV, $\varphi_{K^+} = -12$ mV, and $\varphi_L = +10$ mV. On the other hand, the conductivities of the membrane with respect to potassium and sodium, g_{Na^+} and g_{K^+}, can vary with time; their dynamics is defined as follows: for conductivity with respect to sodium, two dynamic variables, denoted by m and h, are introduced and the following relation is postulated:

$$g_{Na^+} = \bar{g}_{Na^+} \cdot m^3 h;\ \bar{g}_{Na^+} = 0.12\ \Omega^{-1}\ cm^2, \tag{6}$$

where $\bar{g}_{Na^+}$ is the maximum possible conductivity. On the other hand, m and h satisfy the relaxation equation in which the coefficients (which are different for m and h) depend on the potential:

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m, \tag{7}$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h. \tag{8}$$

The dynamics of the conductivity of the membrane with respect to potassium is formulated in an exactly similar way:

$$g_{K^+} = \bar{g}_{K^+} n^4,\ \bar{g}_{K^+} = 3.6 \cdot 10^{-2}\ \Omega^{-1}\ cm^{-2}, \tag{9}$$

and the dynamic variable n satisfies an equation analogous to Eqns. (7) and (8):

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n. \tag{10}$$

By fixing the potential on the membrane and by separating the sodium and potassium currents, Hodgkin and Huxley

found the required form of the relation between the coefficients α_i and β_i ($i = m$, n, or h) on the one hand and the potential on the other:

$$\alpha_m = 0.1\,(\varphi - 25)\,[1 - \exp(2.5 - 0.1\,\varphi)]^{-1}, \quad (11)$$

$$\beta_m = 4\exp(-\varphi/18); \quad (12)$$

$$\alpha_h = 0.07\exp(-0.05\,\varphi); \quad (13)$$

$$\beta_h = [1 + \exp(3 - 0.1\,\varphi)]^{-1}; \quad (14)$$

$$\alpha_n = 0.01\,(\varphi - 10)\,[1 - \exp(1 - 0.1\,\varphi)]^{-1}; \quad (15)$$

$$\beta_n = 0.125\exp(-\varphi/80). \quad (16)$$

In Eqns. (11)–(16) the coefficients α and β have the dimensions of the reciprocals of milliseconds and the potential is expressed in millivolts and is reckoned from the so called rest potential, defined as the difference between the internal and external potentials of the fibre at rest and equal to −60 mV.

The main attempts, of which we are aware, at a physical interpretation of the system described by the Hodgkin–Huxley equations are set out below.

III. INTERPRETATION OF THE HODGKIN–HUXLEY MODEL

In fact the problem is to discover the physical significance of the dynamic variables m, n, and h. In the first studies by Hodgkin and Huxley an attempt was already made to treat these variables as the concentrations of transferring species. Subsequent experiments showed that ion transport across biological membranes is not achieved with the aid of transferring species but takes place via ionic channels. However, an action potential was recently obtained on two-layer lipids membranes under conditions where the mechanism involving mobile transferring agents is extremely probable[12]. It is therefore useful to consider briefly the nature of excitability in a simple example[13].

Adsorption Inhibition of a Transferring Agent

Suppose that the ions A and B can cross the membrane with the aid of different transferring agents T and M. We shall assume that the solution contains a substance X which can bind the transferring agent T on the surface of the membrane. Then the partial voltage–current characteristic of the ion A is

$$I_A = (1 - \Gamma)\,I_A^*(\varphi), \quad (17)$$

where I_A^* is the voltage-current characteristic in the absence of the inhibitor and Γ the fraction of bound transferring agents.

The equation for the membrane potential is

$$C\frac{d\varphi}{dt} = -(I_A + I_B) + I, \quad (18)$$

where I is the external current. The fraction of bound transferring agents is described by the equation of adsorption kinetics:

$$\frac{d\Gamma}{dt} = \alpha(1 - \Gamma) - \beta\Gamma; \qquad \alpha = k_1 e^{z\varphi/s}, \quad \beta = k_2 e^{-z\varphi/s}. \quad (19)$$

We shall examine the special case where the partial voltage–current characteristics are arranged as shown in Fig. 1. The isoclinic lines for this system of equations are presented in Fig. 2*a*. In this case the point of intersection represents the unique stable stationary state. However, the system possesses threshold properties and is capable of generating single pulses. If the system is deflected sufficiently from the state of equilibrium, its subsequent motion will be described by the dashed line in Fig. 2*a*.

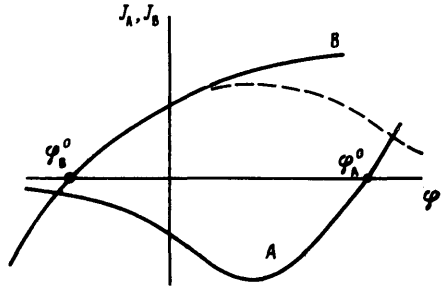

Figure 1. Partial characteristics of the ions A and B. The intercepts made by the curves on the abscissa axis define the equilibrium potentials φ_A^0 and φ_B^0. The dashed line represents the possible variation of I_B.

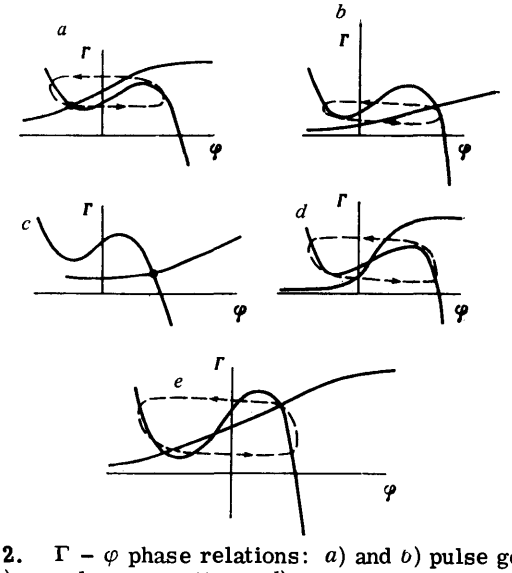

Figure 2. $\Gamma - \varphi$ phase relations: *a*) and *b*) pulse generation; *c*) no pulse generation; *d*) auto-oscillations; *e*) transitions from one stable state to another. The dashed line illustrates the phase trajectories.

In case *b* (Fig. 2) the situation is analogous except that the "action potential" has a different sign. In case *c* the stationary state is stable but the generation of a pulse is impossible, since whatever the deviation from the state of rest the system returns to the latter. In case *d* the only stationary state is unstable, since an auto-oscillatory process takes place in the system. In case *e* there are three stationary states, of which the extreme ones are stable and the intermediate one is not. By a stimulus

exceeding the threshold value, the system can be transferred from one stable state to another, where it can remain indefinitely.

We have analysed the behaviour of the membrane potential in the presence of an inhibitor, the surface concentration of which played the role of a dynamic variable. Another model of an excitable membrane, in which there are no inhibitors but significant diffusion-dependent restrictions are imposed on one of the ions in the layer of solution near the membrane, has been investigated in an analogous manner[13].

Ionic Channels

We shall consider, for example, the potassium channel which "opens" on simultaneous "activation" of four species which do not interact. The rate constants for "activation" α_n and "inactivation" β_n depend on the potential. When these rate constants are interpreted by Eyring's procedure, we have for the constant α_n in the range of negative potentials

$$\alpha_n = e^{2.5\, e\frac{\varphi}{kT}}.$$

Hence it follows that the potassium channel is "activated" when a certain hypothetical species overcomes an activation barrier with a height of $2.5e\varphi$. If the activation is achieved with migration of the charged species in the direction of the force driving the current, then such activation may be attained by transferring a species with a charge of $2.5e$ through the entire thickness of the membrane. On the other hand, when the activation occurs with partial charge transfer, say over a distance $\epsilon\delta$, where δ is the thickness of the membrane, then the field could execute the required work by transferring the $2.5e/\epsilon$ charge between points corresponding to the potential difference $\epsilon\varphi$ (in terms of the constant field approximation). If the elementary displacement amounts to, for example, 5 Å, then $\epsilon = 1/20$ and the charge transferred will be equal to 50 electronic charges or 25 electronic charges when $\epsilon = 1/10$. Both versions are relatively unsuitable from the physical standpoint. The large charge might be accounted for by attributing its displacement to many species and not to a single species. However, in this case the problem would then arise of the explanation of the rigid linkage between these species, because the required potential relation $\alpha_n(\varphi)$ would arise only if the possibility of an asynchronous migration of the species were ruled out.

Below we shall consider in detail one of the cooperative models, but now we shall formulate a convenient method for describing excitable ionic channels in terms of transitions between different conformational states[6]. For brevity, we shall confine ourselves to the potassium channel, since there is no difficulty in extending the treatment to the sodium channel. We postulate that the potassium channel contains x identical independent subunits, each of which can exist in one or two states—0 ("passive" state) and 1 ("active" state). The channel conducts only when all x subunits are in state 1.

Consider an assembly of N identical channels. It is possible to introduce a concentration of channels in which the number of subunits in state 0 is i. It will be designated by c_i. Evidently we have c_0, c_1, ..., c_x, in all $x + 1$ concentrations, corresponding to $x + 1$ different states of the channel. Denoting the rate constant for the transition from 0 to 1 by α and that for the transition from 1 to 0 by β, we obtain a system of equations describing the kinetics of the changes in the concentrations:

$$\left.\begin{aligned}
&\frac{dc_0}{dt} = \alpha c_1 - \beta x c_0;\\
&\frac{dc_1}{dt} = 2\alpha c_2 + \beta x c_0 - \alpha c_1 - \beta(x-1)c_1;\\
&\cdots\cdots\cdots\cdots\cdots\\
&\frac{dc_j}{dt} = -j\alpha c_j + (x-j+1)\beta c_{j-1} - (x-j)\beta c_j + \alpha(j+1)c_{j+1},\\
&\cdots\cdots\cdots\\
&\frac{dc_x}{dt} = -x\alpha c_x + \beta c_{x-1}.
\end{aligned}\right\} \quad (20)$$

By considering the coefficients α and β as functions of the potential, it is possible to describe by Eqns. (20) experiments in which the potential is fixed, because, within the framework of our scheme, the conductivity varies in proportion to the concentration c_0: $g_K = Ng_0c_0$.

We shall now define the steady-state distribution of channels between the states. Putting $d/dt = 0$ in Eqns. (20), we have

$$\left.\begin{aligned}
&\bar{c}_1 = x\frac{\beta}{\alpha}\bar{c}_0 \equiv x\zeta\bar{c}_0;\\
&\bar{c}_2 = \frac{x-1}{2}\zeta\bar{c}_1 = \frac{x(x-1)}{2}\zeta^2\bar{c}_0;\\
&\cdots\cdots\cdots\cdots\cdots\\
&\bar{c}_j = \frac{x!}{(x-j)!\,j!}\zeta^j\bar{c}_0 = c_x^j\zeta^j\bar{c}_0\ ,
\end{aligned}\right\} \quad (21)$$

where a bar over symbol denotes a steady-state value of the given quantity. From the condition

$$\sum_{i=0}^{x} c_i = 1\ , \quad (22)$$

we find

$$\sum c_x^j\zeta^j\bar{c}_0 = 1; \quad (23)$$

hence we have

$$\bar{c}_0 = \frac{1}{(1+\zeta)^x}\ . \quad (24)$$

Thus, after introducing the definition

$$n = \frac{\alpha}{\alpha+\beta} = \frac{1}{1+\zeta}\ , \quad (25)$$

it is immediately seen from Eqn. (24) that, when $x = 4$, the expression for $\bar{c}_0$ is the same as the Hodgkin–Huxley equation for conductivity. Therefore one can write

$$c_0 = n^x.$$

When an experiment with a fixed potential is considered, we have the following solution of Eqn. (10):

$$n = n_\infty - (n_\infty - n_0)e^{-\lambda t}, \quad (26)$$

where $\lambda = \alpha + \beta$. Therefore the conductivity under the conditions of a fixed potential is given by

$$g_K = Ng_0[n_\infty - (n_\infty - n_0)e^{-\lambda t}]^x. \quad (27)$$

When $x = 4$, this expression is exactly the same as the Hodgkin–Huxley equation, provided that we put $\alpha = \alpha_n$ and $\beta = \beta_n$.

Eqns. (24) and (27) confirm that the kinetic scheme described can be regarded as a physical interpretation of the Hodgkin–Huxley model. However, until recently it was impossible to test this scheme directly. The spectra of current fluctuations, which should in principle throw light on the validity of the kinetic scheme, were measured

a comparatively long time ago[14,15]. However, the spectrum usually measured varied with the reciprocal of the frequency $1/f$. This type of variation could not be obtained not only in the Hodgkin–Huxley scheme but also in any other. Therefore it was not certain that the measured quantities are associated with the fluctuations in the conductivity of ionic channels. In 1973 Fishman[7] measured the spectrum of the conductivity fluctuations of the potassium channel, having defined it as the difference between the fluctuation spectra of a normal membrane and a membrane with blocked potassium channels. His spectrum had a density defined by

$$G(\omega) = \frac{f_1(\varphi)}{\lambda^2 + \omega^2}; \quad \omega = 2\pi f,$$

where $\lambda = \alpha_n + \beta_n$ and $f_1(\varphi)$ is a function. These experiments enabled Chen and Hill[6] to compare Hodgkin's kinetic scheme with Fishman's experiments, which led to the observation of a discrepancy between the theory and experiment: the theoretical variation of the critical frequency λ with potential was described by a line lying appreciably above the experimental points (the critical frequency was determined from the point of intersection of the zero and infinite asymptotes in the plot of G against $\ln\omega$). This discrepancy was appreciably reduced by Chen and Hill[6], who assumed the possibility that the current may be conducted by the potassium channel not only in state 0 but also in others. The comparison of Hodgkin's scheme with the results of fluctuation analysis has so far been merely in the nature of a preliminary step. However, it is already clear that fluctuation analysis will be one of the most important instruments for the investigation of the nature of excitability.

IV. GATING CURRENTS

There have been considerable advances in recent years in the elucidation of the physical nature of the excitation process. The brilliant experiments of Armstrong, Bezanilla, Keynes, Rojas, Meves, and others[8-11], led to the observation of asymmetric currents, all the characteristics of which show them to be migration currents of the charged species within the membrane. There is reason to believe that these currents are directly related to the migration of charged groups controlling the conductivity of the sodium channel.

In view of the importance of the problem, it is necessary to define briefly the so called gating current. In the method with fixation of the potential, a membrane incapable of transmitting ions is maintained at a certain potential. Next a potential pulse with a specified amplitude (about 150 mV) and of sufficient duration is applied, the resulting current is recorded, and, after the cessation of the potential pulse, the system is again maintained at the initial potential. Next, a potential pulse of the opposite sign is applied; this leads to a new record of the current as a function of the time elapsed from the beginning of the pulse. The so called gating current is obtained by subtracting the currents corresponding to the same time from one another. The sign of equality then naturally depends on the initial potential and for a certain value of the latter the amplitude of the gating current is zero[9]. It is remarkable that an approximate agreement between the characteristic time of the change in the gating current and the time of the change in the variable m has been observed experimentally over the entire range of potentials. On the other hand, no indication has been obtained of any correlation between the gating current and the variables h and n. Apparently this cannot be accounted for by the inadequate accuracy of the measurements—it is better to change the hypothesis concerning the kinetics of the activation of the sodium current and to seek an appropriate kinetic scheme.

V. THE COOPERATIVE DIPOLE MODEL

The interpretation of gating currents in the Hodgkin–Huxley scheme is based on the hypothesis that several charged groups, which are a constituent part of the channel, migrate through the entire thickness of the membrane. From the physical standpoint, this assumption is unlikely. It is more reasonable to postulate that there is a reorientation of dipoles surrounding the channel, which is equivalent to the transport of a charge across the entire membrane. Then the gating current reflects the rearrangement of the system of dipoles. It differs from the usual displacement current by the asymmetry of the sign of the field. The system of dipoles must be cooperative, since otherwise it would be impossible to explain the marked dependence of the electrical characteristics on the potential.

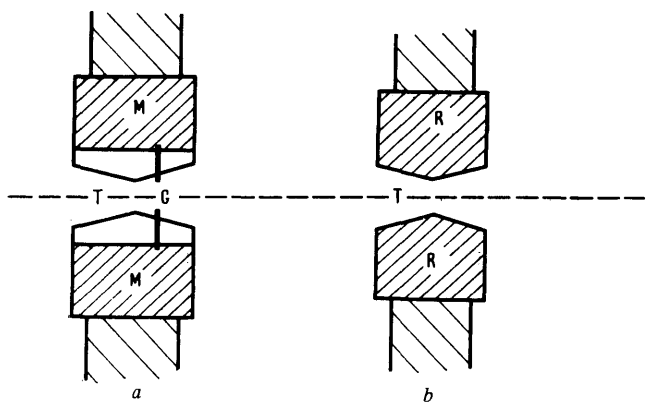

Figure 3. Model of the excited ion channel: *a*) regulation by the alteration of the molecular geometry of the transport system T (M—measuring device; G—gate); *b*) electrostatic scheme for the regulation of conductivity; rigid geometry of transport system; R—regulation system.

The change in the permeability to ions in the course of the reorientation of dipoles may be due to various causes. If the reorientation is coupled with appreciable conformational changes in the system, then the "opening" or "closing" of the channel can have the significance of a change in its molecular geometry. Another case is also possible, where the dipole reorientation influences the electrostatic component of the energy of the ions in the channel, without altering its geometry, and hence influences the concentration of the ions in the membrane and their effective mobility[16].

Models of the channel constructed taking into account the above possibilities are illustrated in Fig. 3. The ion channel probably consists of the transport system proper

(T) and the system regulating the permeability (R). The R unit can include a device measuring the field on the membrane (M), which is linked via certain degrees of freedom with the "gate" (G), i.e. with mobile molecular groups which alter the geometry of the transport system (Fig. 3*a*). There are so far no data which would provide an answer to the question whether the gate is localised or whether the rearrangement involves a considerable proportion of the transport system. Fig. 3*b* represents the electrostatic version of the regulation. There is no point in separating the measuring system from the gate proper, since the geometry of the transport system is assumed to be rigid and the R unit measures the field and regulates the permeability simultaneously. In any of these models the so called gating current is associated with the dipole reorientation in the R or M system. The problem of the calculation of the gating current is entirely independent and requires no hypotheses concerning the mechanism of the regulation of permeability.

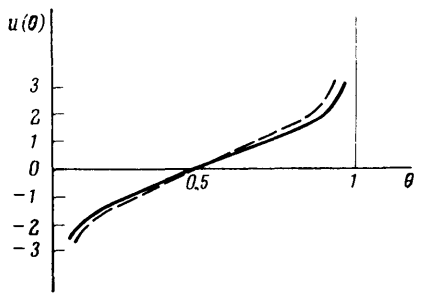

Figure 4. Variation of the cooperative energy of the subunit with θ. The continuous curve corresponds to $\epsilon = 0.2$ and the cooperativity parameter $w = 3.5$. Dashed line—$\epsilon = 0.05$ and $\omega = 3.88$; the phase transition takes place when $w = 4$.

We shall assume that the R (or M) system of the ion channel consists of a large number of subunits, each of which has a dipole moment. Suppose that each subunit can be in one of three states (0, 1, or 2), which differ in the magnitude of the projection of the dipole moment on the axis of the channel and correspond to the transition of the latter from the state of rest to activation and inactivation. In the quasichemical approximation the energy of the subunit in the ith state $V_i(\theta_1, \theta_2, \varphi)$ can be formulated as follows:

$$V_i = w_i(\theta_1, \theta_2) + \varepsilon_i(\theta_1, \theta_2)\,\psi, \tag{28}$$

where $\psi = e\varphi/kT$ is the membrane potential, ϵ_i the effective displacement of the charges in units of the thickness of the membrane, θ_i the degree of filling of the ith state, and w_i the cooperative component of the energy. The rate constants for the transitions are expressed as usual in terms of the differences between the energies of the states, for example:

$$k_{01} = Ae^{\alpha(u_1+\varepsilon_1\psi)};\ u_1 + \varepsilon_1\psi = V_0 - V_1. \tag{29}$$

It is easy to formulate kinetic equations within the framework of the linear scheme:

$$\dot{\theta}_i = -(k_{i1} + k_{i0})\,\theta_i - k_{ij}\theta_j + k_{ij};\ i, j = 0, 2;\quad i + j = 2. \tag{30}$$

We shall confine ourselves to the case of two states, which corresponds to the activation of the ion channel. Assuming that $\theta_2 = 0$, we obtain from Eqn. (30) the equation

$$\dot{\theta}_0 = -(k_{01} + k_{10})\,\theta_0 + k_{10}, \tag{31}$$

the steady-state solution of which has the form analogous to the familiar Frumkin isotherm:

$$\frac{\theta_1}{1-\theta_1}\,e^{-u(\theta_1)} = \frac{A}{B}\,e^{\varepsilon\psi};\ \theta_0 = 1 - \theta_1. \tag{32}$$

According to the experimental data[9], the charge displacement on activation of the sodium channel is described satisfactorily by the formula

$$\theta(\psi) = \frac{1}{1 + e^{-z\psi}};\quad z = 1, 3. \tag{33}$$

Fig. 4 illustrates the $u(\theta)$ relations for different values of ϵ found from the condition that Eqns. (32) and (33) become identical. It follows from Fig. 4 that, in the region of moderate degrees of saturation, $u(\theta)$ is represented satisfactorily by a linear function with cooperativity constants of 3.88 ($\epsilon = 0.05$) and 3.5 ($\epsilon = 0.2$). For low and high degrees of saturation, the cooperativity is still greater.

Fig. 5 illustrates the steady-state $\theta - \psi$ curve obtained for the linear approximation $u(\theta) = 3.5\ (\theta - 0.5)$. Thus, even a slight reorientation of small dipoles yields the required slope of the $\theta - \psi$ curve as a result of the marked cooperativity.

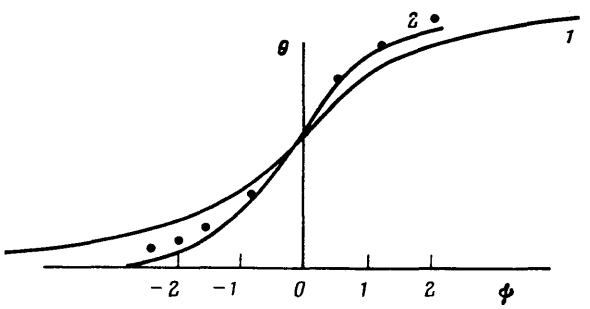

Figure 5. The fraction of transferred charge as a function of potential. Curve *1* was plotted on the basis of Eqn. (32) with a linear fit to the function $u(\theta)$. Curve *2* was calculated by Eqn. (33); circles—experimental data[9].

In order to calculate the gating current, it is necessary to determine the time variation of θ. This relation is illustrated in Fig. 6 for $\alpha = 1$. In this case the $\theta - t$ relation is quasiexponential at a fixed potential. The gating current is found by differentiating the expression for the $\theta(t)$ function.

The method for the determination of conductivity depends on the version of the model of the channel considered—that in Fig. 3*a* or 3*b*. In the former case it is possible to find the conductivity by fitting the function $\varphi(\theta)$ on the basis of experimental data. This procedure is analogous to the selection of the power function ($g_{K^+} \propto n^4$ and $g_{Na^+} \propto m^3h$) in the Hodgkin-Huxley model. In the

second case it is possible to find the form of the $g(\theta)$ function from physical considerations by calculating the concentration of carriers in the channel and the conductivity from the formulae:

$$c \simeq \bar{c} \cdot e^{F}; \; g \simeq c, \tag{34}$$

where F is the change in the energy of the ion in the channel on reorientation of the dipoles, which can be readily estimated:

$$F \simeq \frac{eQ\delta\xi}{4\pi kTSN}(1-\theta). \tag{35}$$

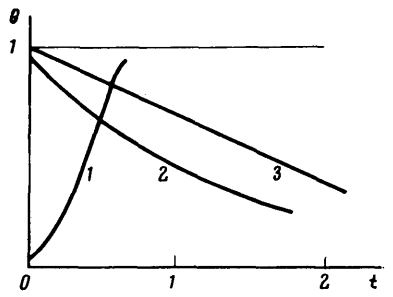

Figure 6. Variation of θ with t: 1) "direct clamp" from $\theta = 0.05$ to $\theta = 0.95$; 2) "reverse clamp" from $\theta = 0.95$ to $\theta = 0.05$; 3) variation of $\lg\theta$ with t corresponding to curve 2.

Here $Q\delta$ is the total change in the dipole moment ($Q \propto 2 \times 10^3 e/\mu^2$), S is the area of the lateral surface of the channel, N the density of the channels, and ξ the structure factor. When $\xi \simeq 10^3$, the energy $F \simeq 10\theta$. Calculations show that there is a great similarity between the variation of θ^4 and $e^{6(\theta-1)}$ in the region of moderate values of θ. The exponential relation between conductivity and θ has the advantage that it makes it possible to explain readily, by the additivity of the energy, the formula $g_{Na^+} \simeq m^3h$ and also the shift of the conductivity current maximum relative to the gating current maximum.

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Anodic Dimerisation, Addition and Substitution Reactions of Organic Compounds

L.A.Mirkind

The review deals with certain general characteristics of the behaviour of organic substances at high positive potentials, which determine the mechanism and kinetics of anodic dimerisation (condensation), addition, and substitution reactions. A systematic account is given of the most significant results of studies in recent years on organic electrosynthesis based on the above classes of reactions.
The bibliography includes 303 references.

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I. INTRODUCTION

There has been a considerable growth in recent years of research on anodic dimerisation (condensation), addition, and substitution reactions dealing with the study of the kinetics and mechanism of anodic processes and with the development on the basis of the above classes of reactions of effective methods for the electrochemical synthesis of various monofunctional and polyfunctional compounds which are valuable intermediates in many branches of polymer chemistry and organic synthesis. Since a systematic account has been given of the data accumulated in 1970–1971 in a number of special reviews dealing with the problem as a whole [1-3] or with individual classes of reactions [4-8], we shall confine ourselves to the consideration of the results in later publications, concentrating attention on general characteristics and also on certain problems concerning which there is still controversy in the literature.

The enhanced interest in the study of reactions of the above classes has been aroused primarily by the fact that the electrochemical methods for carrying them out have many advantages over chemical methods [9,10].

1. The anodes used for the oxidation (platinum, graphite, lead dioxide, etc.) are inert, in contrast to chemical oxidising agents which give rise to undesirable side reactions. There is also no need for the subsequent separation of the oxidant reduction products.

2. The possibility of a smooth variation of the potential within wide limits makes it possible to achieve selective reactions in the presence of several oxidisable groups or of degrees of oxidation and also to carry out oxidations in the same apparatus under conditions ranging from very mild to very severe.

3. It is easy to control the changes in the nature and rate of formation of the intermediate species by regulating the potential and anodic current density and by modifying the electrical double layer, which makes it possible to generate under mild conditions high local concentrations of such species in the vicinity of the electrode and this frequently facilitates a selective or specific course of the reaction.

4. Since the electron transfer is determined by the changes in the anodic potential, the temperature can be in many instances freely selected, which is also an important preparative advantage†.

The above characteristics are responsible for the specific features of the reaction pathways and the products formed in anodic reactions and in many cases make it possible to achieve processes which either have no chemical analogues or lead to the same products in a simpler way. As an example one may quote the reactions of organic-inorganic synthesis in the electrolysis of mixtures of organic (acetic, propionic) and inorganic (sulphuric, perchloric, nitric) acids [11-14]. At low temperatures (−20°C) and high potentials ($\varphi \geqslant 3.0$ V) peroxy-compounds having the general formula $RCOOOR_1$ are formed at a platinum anode in concentrated acid solutions:

$$RCOO^- + R_1O^- \xrightarrow{-2e} RCOOOR_1;$$
$$R=CH_3,\ C_2H_5;\ R_1=SO_3H,\ ClO_3,\ NO_2\ .$$

The chemical procedures for the preparation of such substances are fairly complex.

There are also no chemical analogues of addition reactions such as the carboxydimerisation of conjugated dienes resulting in the formation of higher unsaturated dicarboxylic acids [15]:

$$2\,(HOOC)_2 + 2\,C_nH_{2n-2} \xrightarrow{-2e,-2H^+,-2CO_2} HOOC\,(C_nH_{2n-2})_2\,COOH;$$

the synthesis of dicarbonyl compounds in the oxidation of sodium dimethylmalonate and sodium acetylacetonate in the presence of styrene or ethyl vinyl ether [10,16] ($k = 1$ or 2):

$$2\,(RCO_k)_2CH^- + \rangle\!=\!\langle^{Y} \xrightarrow{-2e} (RCO_k)_2CH\left(\begin{array}{c}Y\\|\\|\end{array}\right)_k CH\,(CO_kR)_2;$$

and the anodic aroyloxylation of 1,3-dienes [17,18]:

$$2\ XArCOO^- + C_nH_{2n-2} \xrightarrow{-2e} XArCOOC_nH_{2n-2}OOCArX;$$
$$X=C_nH_{2n+1},\ C_nH_{2n+1}OOC,\ OH\ .$$

† Reactions involving unstable radicals, for example $RCOO^{\cdot}$, the occurrence of which is promoted by low temperatures, constitute an exception [14].

The unusual features of the reaction pathways in anodic processes of the above classes are determined in many respects also by the fact that at least the individual stages of these processes are electrocatalytic, since they occur at an interface and depend significantly on the state of the electrode surface.

II. CERTAIN CHARACTERISTICS OF ANODIC PROCESSES AT HIGH POSITIVE POTENTIALS

The majority of anodic dimerisation, addition, and substitution reactions require comparatively high positive potentials (1.5–3.5 V) and, in order to understand their mechanism, it is necessary to take into account many common features of electrode processes under these conditions.

At high anodic potentials the oxidation of the substrate is in most cases accompanied by the oxidation of the solvent usually employed (water, lower aliphatic alcohols, acetone, etc.). Under these conditions, there is a change in the state of the electrode surface and in the composition and bonding energies of the adsorbed components of the electrolyte and the oxidation intermediates, which is inevitably reflected in the direction or relative rates of secondary chemical reactions.

The water in the electrolyte, which is almost always present as an impurity even in dried organic solvents, leads to the liberation of oxygen, accompanying the oxidation of the organic substance. On platinum metals (which are most frequently used), certain oxides are formed, which alter sharply the adsorption and catalytic properties of the surface and lead to a decrease of the effective potential in the zone corresponding to the formation of the transition state of the species undergoing oxidation.

It is therefore reasonable that, in the study of the mechanisms of such reactions, it is necessary to take into account in the first place the influence of heterogeneous factors on the rate and direction of electrode processes. It is also necessary to discover whether chemical reactions preceding electron transfer (including those accompanied by the adsorption of the neutral substrate or oxidation intermediates) occur and also the requirements for the orientation of the molecule on the electrode surface and the preferred orientation. It is essential to determine the nature of the oxidant (the electrode itself, oxygen, or the intermediates in the oxidation of water and OH^- ions), the species being oxidised, and the intermediates formed initially (radicals, radical-ions, or ions), and the sequence of stages in their reactions.

In certain cases it is possible to determine the nature of the primary product formed on the electrode by direct measurements. For example, the formation of phenylacetoxy-radicals in the oxidation of phenylacetic acids in acetonitrile has been demonstrated[19,20] by ESR; the influence of the solvent on the hyperfine structure of the spectrum indicates the stabilisation of the radicals by solvation effects. The formation of adsorbed phenoxy-radicals in the oxidation of sterically hindered phenols (SHP) on a graphite electrode over a wide pH range has been demonstrated by ESR.[21] This finding shows that, in both alkaline and in acid and neutral solutions, the primary step in the electrochemical oxidation of SHP is a one-electron transition. Analysis of the ESR spectra in the oxidation of substituted phenols on platinum and of stable phenoxy-radicals on graphite leads to a similar conclusion[23].

However, the above problems have not been fully elucidated for any reaction of the classes under consideration, largely because of experimental difficulties associated with the study of electrode processes and potentials in excess of the reversible oxygen potential (φ_0). In most cases the methods used as low potentials for the unoxidised metal are insufficiently effective under these conditions and the adsorption and kinetic characteristics discovered for dilute aqueous solutions of simple organic substances at $\varphi < \varphi_0$ [22] cannot be reliably extrapolated to this region[2,3,24,25]. When non-aqueous solvents are used, addition complications arise.

Nevertheless vigorous studies in recent years of new methodological approaches to the investigation of electrode processes under these conditions and the combined application of various electrochemical[26-41], optical-spectroscopic[42-48], radiochemical[49-56], mass-spectrometric[57], electron diffraction[58-60], and conductimetric[61] methods together with methods based on the identification of the products of potentiostatic electrolysis[2,3,62-64] have already made possible certain qualitative or semiquantitative generalisations. This applies in the first place to problems concerning the state of the electrode surface (mainly the platinum electrode) over a wide range of potentials and its influence on the direction and rate of electrochemical reactions. However, most of the studies have dealt with inorganic systems. Among these mention should be made in the first place of the series of investigations by Veselovskii, Kasatkin, Yakovleva, and coworkers on the synthesis of oxidants at high positive potentials[63,64] and also by Tyurin and coworkers on the oxygen evolution reaction on platinum metals[26-29,65-68]. Among reactions involving organic substances, only the electrochemical oxidation of carboxylates has been studied in this way[69].

Numerous experimental data confirming the thesis of the decisive influence of the compositions and properties of surface compounds of the electrode with the components of the solution and the intermediates in the electrochemical oxidation on the direction and rate of electrode reactions at $\varphi > \varphi_0$ have now accumulated. Unfortunately in most of the studies devoted to preparative organic electrochemical synthesis at high anodic potentials this factor has so far been ignored and the conclusions concerning the mechanism are reached mainly on the basis of a comparison of the composition of the products of the electrolysis and the corresponding chemical reactions. The necessity to take into account the characteristics of the surface phenomena, in particular the adsorption processes at the electrode/solution boundary, has been acknowledge in only a few studies carried out in recent years[70-78].

The $i-\varphi$ curves and the variation of the double layer capacitance, the adsorption pseudocapacitance, and the polarisation resistance with the potential, measured in solutions of different compositions at platinum metals, gold, and graphite, exhibit sharp breaks, maxima, and minima. As an illustration, Fig. 1 presents $\lg i-\varphi$ curves for a solution of monomethyl glutarate in methanol using gold (curve *1*), iridium (curve *2*), rhodium (curve *3*), platinum (curve *4*), pyrographite (curve *5*), and vitreous carbon (curve *6*)[77] electrodes, while Fig. 2 illustrates the variation of the double layer capacitance with potential at smooth platinum in 1 *N* H_2SO_4 solutions with added $n\text{-}C_5H_{11}COOH$ obtained by an a.c. bridge method[28].

In many cases the reaction is inhibited by the electrolyte component which begins to be oxidised vigorously at a value of φ more positive than that corresponding to the potential jump or current (capacitance) drop. Fig. 3 presents plots of polarograms, in terms of semilogarith-

mic coordinates, recorded at a rotating platinum anode in alkaline solutions of pelargonic acid[78]. Evidently, with increase of the concentration of the carboxylate anion, the oxidation of which with formation of hexadecane takes place mainly at potentials corresponding to section V, there is a decrease of both the potential and the maximum current of the discharge of the OH^- ion—the dominant oxidation process along the lower sections.

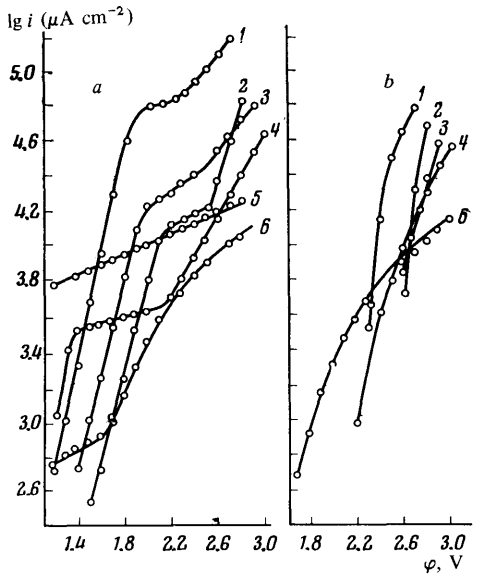


Figure 1. Anodic polarisation curves (*a*) and partial polarisation curves (*b*) for the oxidation of monomethyl glutarate in a methanol solution of 0.3 M $CH_3OOC(CH_2)_3$. .$COONa$ + 1 M $CH_3OOC(CH_2)_3COOH$ on electrodes made of different materials.

The adsorption of stable final or intermediate products[79,80] and the electrolyte anions[81,82], the change in the rate-determining stage[83-86], and the formation of surface oxides[26-29,38,64,88] have been considered in the literature as the probable causes of the inhibition of electrochemical oxidation and of the change in the properties of the interface in various systems. In many instances the relation between the surface coverage, the composition and properties of the chemisorbed products of the dissociation of water (OH^-), and the kinetic properties of the oxidation reactions were characterised quantitatively[28,29,38,67,88,90].

A wide variety of surface oxygen compounds of platinum metals and gold are known to exist[91-95]. The number of studies dealing with the nature and stoichiometry of surface oxides, their relative stabilities, the conditions governing their formation and interconversions, and their involvement in oxygen evolution reactions and in oxidation of organic substances greatly increased in recent years. The greatest number of studies have dealt with platinum[24-32,36,38,40,43,48,96-102], much less attention being devoted in this respect to graphite[39,101,104,106], gold[33,37,42,43], palladium[33,52,107], iridium[102,103], ruthenium[102], and rhodium[102,108-110].

Potentiodynamic measurements in solutions of inorganic acids and alkalies[26,27,56,83,85,111,112] have shown that the overall degree of coverage of the surface of smooth platinum by chemisorbed oxygen increases monotonically up to potentials φ_r‡ ≃ 2.1 V and reaches a limiting value (2.3–2.7 monolayers), which no longer changes as the potential is increased further (Fig. 4).[56]§

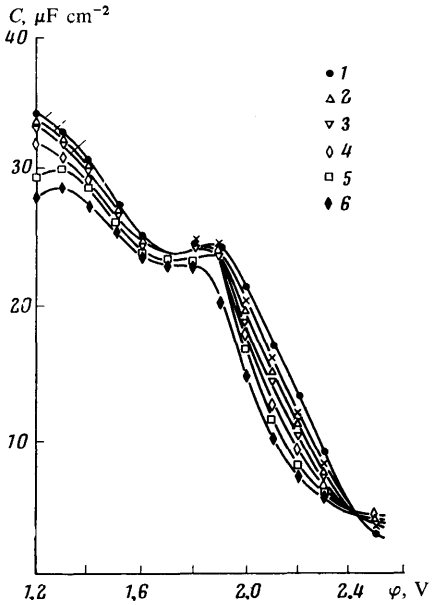


Figure 2. Variation of the double layer capacitance with potential on smooth platinum in 1 *N* H_2SO_4 with added $n\text{-}C_5H_{11}COOH$ at different molar concentrations: 1) 0; 2) 3×10^{-5}; 3) 10^{-4}; 4) 3×10^{-4}; 5) 10^{-3}; 6) 3×10^{-3}.

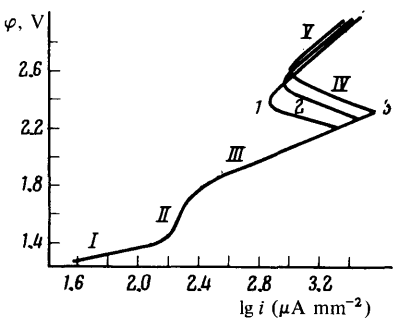


Figure 3. Anodic polarograms obtained on platinum in 0.5 *N* $NaOH + xN$ $CH_3(CH_2)_7COONa$ solutions for different *x*: 1) 1; 2) 0.5; 3) 0.1; the rate of application of potential was 10 mV s^{-1}.

‡ φ_r is the potential relative to the hydrogen electrode in the same solution.

§ Q_O and Q_H are the amounts of electricity consumed in the reduction of oxygen and the "deposition" of hydrogen respectively.

At $\varphi_r = 1.4-1.6$ V monolayer coverage by the oxide is attained, the oxide being reduced at $\varphi_r \simeq 0.6$ V (the so called first form of the oxide); at higher potentials the second form of the oxide is formed, being reduced at hydrogen adsorption potentials ($\varphi_r \simeq 0.2$ V). Multilayer bulk-phase deposits are formed in the range $\varphi_r = 2.1$ to 2.3 V,[26,27,59,113-115], mainly in dilute solutions at an elevated temperature, evidently only after the saturation of the surface by chemisorbed oxide layers and at a small number of active centres on the metal[27]. For both platinum and gold electrodes, a significant change in the properties of the surface oxide with time has been noted, in consequence of the increase of bonding energy or the incorporation of oxygen atoms in the crystal lattice of the subsurface layers of the metal.

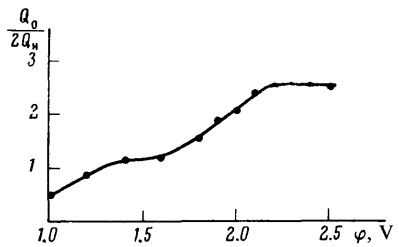


Figure 4. Variation of the degree of surface coverage of smooth platinum by chemisorbed oxygen with potential.

The oxides on platinum belonging to the second form are chemically inert with respect to many organic (and inorganic) substances; an increase of the degree of surface coverage by an oxide of the second form θ_{OII} in the range 1.6–2.3 V results in the inhibition of the electrochemical oxidation of the majority of the compounds investigated, which is reflected in a decrease of the current or an increase of the Tafel slope. The influence of the surface coverage of the platinum electrode by chemisorbed oxygen on the inhibition of the electrochemical oxidation of organic substances has been characterised quantitatively in some investigations[24-29,62,90].

The adsorption of oxygen on platinum at high positive potentials has a competitive mechanism: depending on the concentration and nature of the substance, the fraction of the surface atoms O_{ads} [or other intermediates in the oxygen evolution reaction (OEV)] displaced by the specifically adsorbed inorganic anions, neutral atoms (for example Cl°), or organic compounds changes[24-29,34,35,38,46,65-68,88].

The behaviour of organic substances has been so far inadequately investigated along these lines. In contrast to the range of low potentials, it is much more difficult to determine the structure of the adsorbed species on an oxidised electrode and the nature of their interaction with the surface (associative or dissociative); there are very few data concerning the surface phenomena on electrodes in non-aqueous solvents. The quantitative study of the adsorption of neutral molecules of high potentials involves significant methodological difficulties. These processes are in fact of great importance for the classes reactions under consideration, since it has been shown in recent years[1-3] that the adsorption of a neutral substrate predetermines the efficiency and mode of addition and substitution processes involving short-lived radicals and radical-ions generated on the electrode surface as a result of charge transfer.

III. CHARACTERISTICS OF THE ADSORPTION OF NEUTRAL ORGANIC SUBSTANCES ON OXIDISED PLATINUM

The possibility of the chemisorption of organic molecules on platinum at potentials exceeding significantly that of the reversible oxygen electrode (up to $\varphi_r = 3.0$ V) has been established[116,117] for conjugated dienes and then for other systems[24,25,35,55,118,129]. In recent years this phenomenon has been investigated vigorously by Tyurin and coworkers, who demonstrated the general nature of the adsorption characteristics at high potentials discovered previously[26-29,67,68,133]. It is useful to consider this problem in greater detail, since the existence of this effect is, on the one hand, of fundamental importance for the understanding of the mechanisms of the majority of reactions of the classes being considered and, on the other hand, in many studies it has hitherto been either denied or simply ignored in the discussion of the possible reaction pathways. In the majority of investigations the impossibility of appreciable adsorption of neutral molecules in the range of potentials corresponding to vigorous evolution of oxygen and coverage of the surface by oxides is postulated *a priori*.

On the basis of earlier data[116-119], Kuhn and Sunderland[120] recently investigated the possibility of the adsorption of certain olefins by analysing their oxidation products in aqueous solutions and concluded that the nature of the substances formed (their amount is extremely small owing to the negligible solubility of the olefin) may be interpreted from the standpoint of homogeneous reactions. Therefore, according to the authors[120] the effects observed previously[116-119] may be identified as a result of physical adsorption. It must be emphasised that a one-sided study of the nature of the oxidation products only is hardly a fruitful procedure for obtaining evidence for adsorption and even less so for the determination of its energy characteristics or steric effects. This must be mentioned because such an approach has been widely used recently—for example in studies of anodic substitution reactions with participation of indane[73-76] and stilbene[70] and of the postanodic condensation of carboxylates[71,72], in which unusual directing effects of the substituents and relative amounts of isomeric products were observed. Without casting doubt on the possibility of the adsorption of the substrate in the reactions considered, one must emphasise that such results can be associated also with other features of electrochemical oxidation reactions, for example with a structure which is not characteristic of chemical analogues or with a high local concentration of intermediate species[121,123].

In order to investigate the adsorption of organic substances at high positive potentials, indirect electrochemical methods were mainly used previously, namely coulometric adsorption displacement methods, methods involving a diminution of the capacitance or pseudocapacitance, and the method based on the inhibition of oxidation reactions[2,3]. However, it has been emphasised[2,24,56] that they all suffer from significant limitations and probably yield reliable information only when several are combined. In certaininstances there is a quantitative

correspondence between all the criteria of surface coverage by an organic adsorbate, characteristic of each of these methods, as has been observed, for example, in the adsorption of pentyl alcohol and valeric acid on platinum (Fig. 5).[28] However, all the methods enumerated are based on a number of assumptions. As shown for the adsorption of ethylene[124], aliphatic alcohols[125], and dienes in methanol solutions of oxalic acid[15], cycloalkanes[25,35], and chloride ions[126], they do not always permit an unambiguous interpretation of experimental data, leading to results such as negative adsorption, negative slopes of kinetic isotherms, etc. When the potentiodynamic rapid cathodic pulse method, which has been widely used for adsorption measurements at $\varphi > \varphi_0$, is applied, the conditions governing the correct determination of θ by the integration of $i-\varphi$ curves are not always ensured (and may not hold) since no account is taken of the possible change in the stoichiometry of the displacement[127] and of the influence of the adsorbate on the maximum surface coverage by electrochemically active species and on the kinetics of their reduction under pulsed conditions. The separation of the effects due to the blocking of the active centres of the metal and the inhibition of the reduction of the chemisorbed oxygen is usually difficult[68].

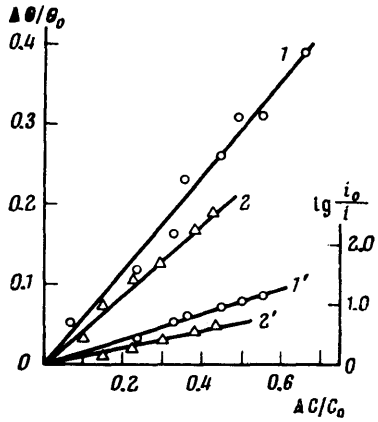


Figure 5. Variation of the inhibition coefficients for the oxygen evolution reaction $\lg(i_0/i)$ (lines *1'* and *2'*) and for the displacement of oxides $\Delta Q/Q_0$ (lines *1* and *2*) with the depression of the capacitance $\Delta C/C_0$ for 1 *N* H_2SO_4 + n-$C_5H_{11}OH$ (lines *1* and *1'*) and 1 *N* H_2SO_4 + n-$C_5H_{11}COOH$ (lines *2* and *2'*) at $\varphi = 2.2$ V; the circles on the straight lines correspond to different concentrations of additives.

It is therefore useful to compare the results obtained by electrochemical methods with data derived from direct adsorption measurements. The fruitfulness of this approach has been emphasised[124]. The study of the adsorption of a number of organic substances has been undertaken[55,56,128-133]: aromatic hydrocarbons[35,55,56], alcohols[128,129], carboxylic acids[53,54,129], and thiourea[130,133] on smooth platinum in 1 *N* H_2SO_4 solutions up to $\varphi_r \simeq 2.5$ V using a combination of electrochemical methods and the ratioactive tracer method. Direct adsorption measurements with the aid of compounds labelled by radioactive isotopes fully confirmed both the very fact of an appreciable adsorption of organic molecules at high positive potentials and the principal quantitative characteristics found previously. Fig. 6[56] illustrates the variation of the surface coverage θ and the degree of adsorption Γ with potential obtained by the potentiodynamic method (lower curves) and with the aid of labelled compounds (upper curves) for benzene and naphthalene. The nature of the curves is basically similar; the differences between them are associated with the fact that the values of θ actually characterise the degree of displacement of chemisorbed oxygen and those of Γ characterise the overall surface excess of the organic substances both within the oxide and on the oxide. Comparison of the measurements by electrochemical and isotopic methods permits conclusions to be made about the stoichiometry of the displacement, the relative distribution of the adsorbed substances in the surface layers, and many other features.

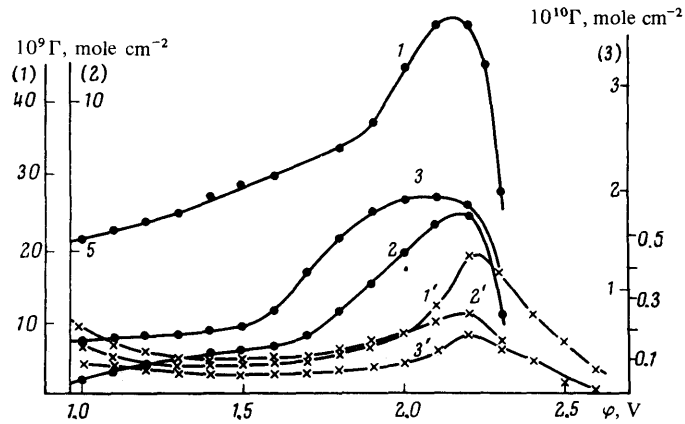


Figure 6. Variation of the degree of adsorption Γ (curves *1–3*) and of the degree of surface coverage θ (curves *1'–3'*) of platinum with potential: 1) and 1') 0.089 M benzene; 2) and 2') 2×10^{-4} M naphthalene; 3) and 3') 0.01 M benzene.

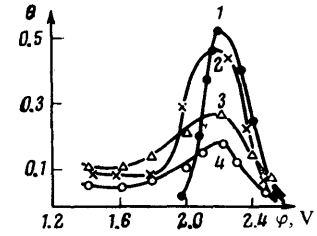


Figure 7. Variation of the degree of surface coverage of platinum by different substances with potential: 1) 5×10^{-4} M cyclohexane; 2) 5×10^{-4} M cyclohexene; 3) 10^{-4} M naphthalene; 4) 10^{-3} M benzene.

Figs. 7 and 8 illustrate the $\theta-\varphi$ and $\Gamma-\varphi$ relations obtained by the potentiodynamic method for hydrocarbons (butadiene, cyclohexene, and cyclohexane)[35] and by the radioactive tracer method for C_{1-6} aliphatic alcohols[128].

The data presented confirm the general nature of the effect of the adsorption of organic substances at $\varphi > \varphi_0$ and show that, apart from the familiar maximum in the double layer region, the $\Gamma-\varphi$ curves have yet another maximum at potentials of 2.1–2.3 V, where the limiting coverage of the platinum anode by chemisorbed oxygen is reached. A similar phenomenon has been observed for oxidised rhodium [108]. The presence of a number of adsorption maxima for smooth platinum has also been confirmed by other data [132-136], according to which there exists yet another region of enhanced adsorption activity of platinum at high positive potentials.

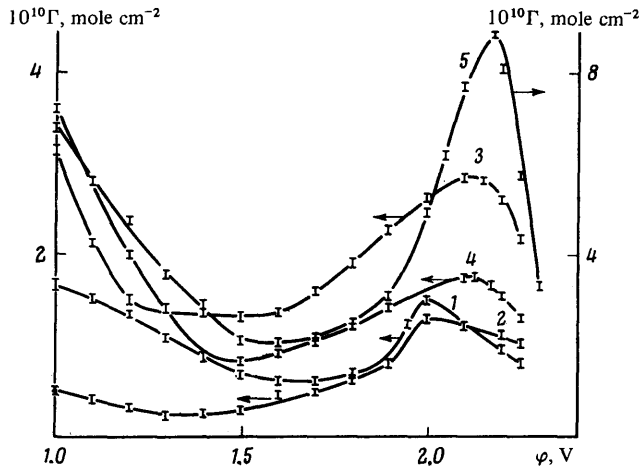


Figure 8. Variation of the degree of adsorption Γ of different substances on platinum with potential: 1) 0.15 M CH_3OH; 2) 0.0532 M C_2H_5OH; 3) 0.1 M i-C_3H_7OH; 4) 0.090 M t-C_4H_9OH; 5) 0.048 M n-$C_6H_{11}OH$.

Analysis of the experimental data accumulated in recent years permits certain generalisations of the characteristics of the adsorption of organic substances on oxidised platinum.

1. The adsorption of organic compounds (at least of the major proportion of the adsorbate) is as a rule irreversible and is accompanied by the displacement of chemisorbed oxygen. The introduction of molecules into the oxide layer stabilises them on the surface. There is a broad overall spectrum of energy states, including weakly bound species [128].

2. In the series of compounds of the same type and having similar molecular weights, those with multiple bonds exhibit a greater adsorbability.

3. In contrast to unoxidised smooth and platinised platinum, on which far-reaching degradation of molecules takes place, the adsorption of organic compounds on the oxidised metal may be manifested as an associative process [2,3,62,137].

4. In contrast to the range of low potentials, for which a logarithmic adsorption isotherm with similar values of the inhomogeneity factor f (Damaskin et al. [22]) is typical, at $\varphi > \varphi_0$ the variation of surface coverage with concentration c is not of a single type. In some cases it is described satisfactorily by the Temkin equation with f depending on the potential and the nature of the substance [62,131]:

$$\theta = \frac{1}{f}\ln(Bc);\ B = \text{const.},$$

while in others (for example, for alcohols [128,135] or acids [129]) the agreement with the Freundlich equation is better (Fig. 9):

$$\theta = Bc^n;\ n < 1.$$

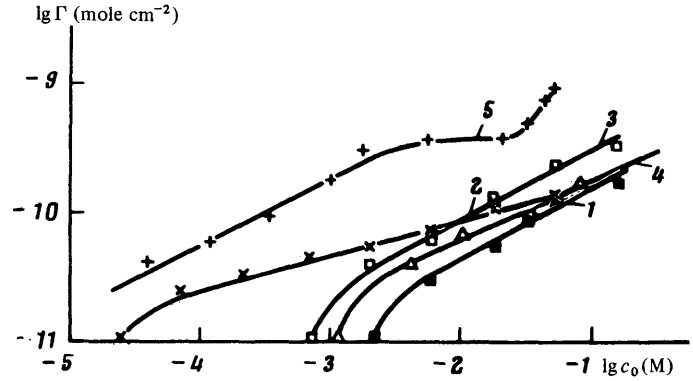


Figure 9. Variation of the degree of adsorption of different substances on platinum at the maximum potentials with the concentration of alcohols in terms of logarithmic coordinates: 1) CH_3OH; 2) C_2H_5OH; 3) i-C_3H_7OH; 4) t-C_4H_9OH; 5) n-$C_6H_{11}OH$.

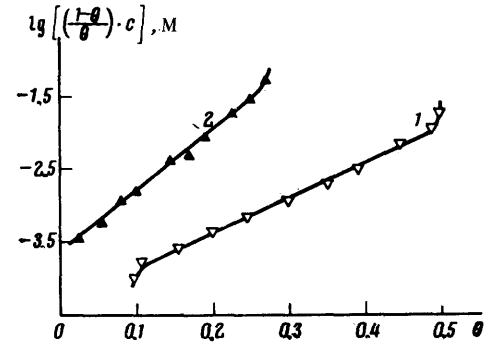


Figure 10. Variation of the degree of surface coverage of platinum with the concentration of buta-1,3-diene at different potentials (V): 1) 2.1; 2) 2.8.

The adsorption of dienes from sulphuric acid solutions obeys the Frumkin equation (Fig. 10): [134]

$$Bc = \frac{\theta}{1-\theta}\exp(f_1\theta);\ f_1 = \text{const}.$$

5. The adsorption kinetics are described by power equations of the Banham–Barth (Kwan) type [128]:

$$\theta = k\cdot\tau^n;\ \tau - \text{time},\ k = \text{const.};$$

or the Zel'dovich–Roginskii type [35,130]:

$$\theta = A + \frac{1}{\alpha f}\ln\tau;\ \alpha \leqslant 1;\ A = \text{const.}$$

6. The formation of multilayer coatings at concentrations differing by not more than an order of magnitude from saturation has been observed for certain substances [55,56]. Fig. 11 [56] presents curves relating Γ and θ to c for benzene and naphthalene; the ascending branches of the curves correspond to the appearance of multilayer deposits. Weber and Loučka also concluded recently that multilayer adsorption is possible (for sulphur on smooth platinum) [138].

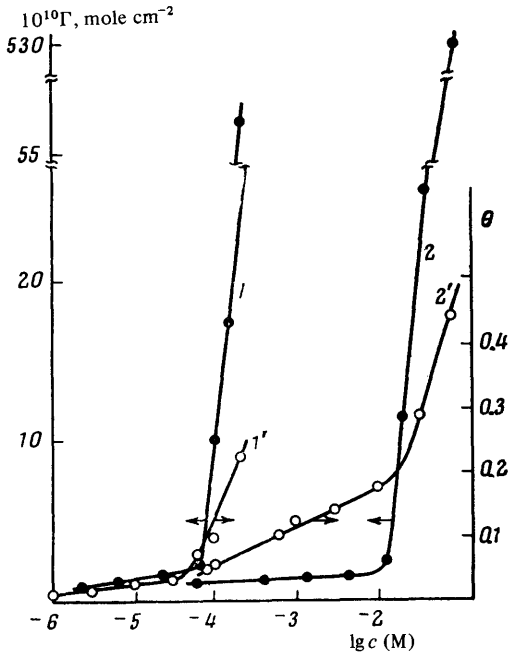


Figure 11. Variation of the degree of adsorption Γ (curves *1* and *2*) and of the degree of surface coverage θ (curves *1′* and *2′*) by different substances with concentration: 1) and 1′) naphthalene; 2) and 2′) benzene.

7. The substance adsorbed on energetically inhomogeneous surfaces of platinum metals and graphite can not only block the active centres but can also have a significant influence on the kinetics of the oxidation and the energy of adsorption on the unoccupied sections. In conformity with the model of the "surface electron gas" [139,140], one can predict both an inhibiting and a promoting influence of the initially adsorbed substance on the rate of discharge and also a change in the metal–adsorbate bond strength on the free sections of the surface.

The sign of the effect will be determined by the nature of the adsorbate and of the oxidation process. Indeed Gileadi and coworkers [141–143] observed the selective inhibition of oxidation reactions by certain compounds, particularly by phenols. The inhibition of the electrochemical oxidation of benzaldehyde and acetophenone (compounds which are readily oxidised by atmospheric oxygen but are resistant to anodic oxidation), reported by Solomin and Kryuchkova [144], probably belongs to phenomena of this type. The authors [144] begin with the following process mechanism (postulating the intermediate formation of benzoyl hydroperoxide, the decomposition of which results in the appearance in solution of a process inhibitor—phenol):

$$C_6H_5CHO \rightarrow C_6H_5COOOH \rightarrow C_6H_5OH + CO_2.$$

Kazarinov and Dolidze observed an appreciable increase in bonding strength and a decrease of the rate of oxidation of methanol adsorbed on platinum together with hexyl alcohol [145].

Effects with a different sign, namely selective promotion of the oxidation of oxalic acid at low coverages of the platinum anode by dienes in alcoholic solutions [15,146] and the stimulating effect of the adsorbate on coverage by oxygen [24,35], have been observed. Similar phenomena were recently noted in the adsorption of submonolayer amounts of noble metals [147] as well as arsenic, sulphur [148,149], mercury, and acetonitrile [150] on platinum. It was shown that, depending on θ and the nature of the substance being oxidised, the reaction is either accelerated or inhibited.

Since the thermodynamic method developed by Frumkin [151–152] and experimentally validated [22] for degassed platinum metals is inapplicable to the analysis of irreversible adsorption processes on oxidised metals, in certain investigations attempts were made to interpret the nature and characteristics of adsorption at high values of φ on the basis of other concepts.

In the first studies carried out in this field [116–119] it was assumed that the high bonding energy between the adsorbate and the metal, which stabilises the latter with respect to oxidation by the oxygen evolved, is due to the presence in the adsorbate molecule of valence-unsaturated groups, the interaction of π electrons of which with the positively charged surface of the anode leads to the formation of stable chemisorbed compounds (of the type of π complexes). The interpretation of the nature of the adsorption effects at high potentials was developed further in studies by Tyurin and coworkers [66,67]. In particular, the authors postulate that the second form of the surface oxide formed on the platinum electrode above 1.5 V is a coordination compound of the metal and the intermediate products of the oxygen evolution reaction and other components of the electrolyte: ions and neutral molecules. All the species enumerated behave as ligands, which compete with one another in the half-sphere of the complex in which the electron-accepting species is Pt^{4+}. Within the framework of this mechanism, the increase of the degree of adsorption in the range 1.5–2.2 V is caused by the increase of the degree of surface coverage $\theta_{O_{II}}$ and its decrease at higher potentials is associated with the increase of the rate of oxidation of the adsorbate. However, it has been noted [3] that both treatments suffer from a number of disadvantages. The complex-adsorption model was improved further in recent investigations [153].

We shall consider next the characteristics of each of the reaction classes discussed taking into account the above considerations.

IV. ANODIC DIMERISATION REACTIONS

The most important of the anodic dimerisation processes is the Kolbe electrochemical condensation of carboxylic acids and its modification—the condensation of dicarboxylic

acid monoesters (the Brown–Walker reaction):

$$2\,RCOO^- - 2e \rightarrow RR + CO_2 .$$

These reactions are of preparative interest for the synthesis of many valuable bifunctional compounds and in many cases there are favourable prospects for their industrial application. This involves the synthesis of sebacic acid diesters by the electrolysis of monoalkyl adipates [154] and also the synthesis of suberic acid by the condensation of monomethyl glutarate [77,159]. A number of reviews have been devoted to the synthetic and kinetic aspects of Kolbe type reactions [3,4,69,154,156,157]. Here we shall note the principal process conditions and also certain trends in the recent research in this field.

The yield of the dimeric product is determined by a number of experimental and structural factors. The dimer is formed mainly at high potentials ($\varphi > 2.1$ V), using smooth platinum, iridium, and graphite anodes in an aqueous medium. The use of non-aqueous solvents promotes condensation; in organic media (alcohols, acetonitrile, dimethylformamide, etc.) the choice of the anodic material is less limited—anodes made of gold, palladium, lead dioxide, and certain other materials are suitable in addition to platinum metals. An increase of temperature and the addition of extraneous electrolytes lead to a decrease of the yield of the dimer. The influence of structural factors is discussed below. The investigation of the influence of a series of experimental conditions on the kinetics of the electrochemical oxidation of monomethyl glutarate on platinum in methanol has been reported [77,155]. In particular, it has been shown that the nature of the anode material does not have a decisive influence on the electrochemical oxidation process. The observed fractional order of the reaction of the monoester shows, according to the authors, that the rate-determining stage is the discharge of the monoester anions (on a uniformly inhomogeneous surface).

A similar conclusion concerning the nature of the rate-limiting stage was reached also in studies on the electrochemical oxidation of propionate in an aqueous medium [160] and of acetate in anhydrous acetic acid [158]. Very low reaction orders $n \ll 1$ were also observed in the oxidation of alkylboronic acids, the electrochemical oxidation reactions of which have much in common with the Kolbe reaction [161]. The influence of the nature of the monoester on the oxidation kinetics in methanol solutions on platinum has been discussed [155]. The principal kinetic features are identical with those observed earlier for monomethyl adipate and acetate [116,117,119], which permits the fully justified conclusion that there is a profound analogy between the kinetics of electrode processes in the Brown–Walker and Kolbe reactions in aqueous and alcoholic solutions of many monocarboxylic acids and dicarboxylic acid monoesters. With increase of the length of the hydrocarbon chain, the adsorbability of the carboxylate anion increases also, as has been observed in aqueous solutions [119]; as a result, the maximum solvent oxidation current falls and there is a linear relation between the logarithm of current density and the number of methylene groups in the molecule. The necessity for the adsorption of the carboxylates on the anode prior to their discharge also follows from the results of a study of a Kolbe cross-reaction (mixed reaction) [71].

The problem of the use of carbon electrodes in the oxidation of carboxylates in various solvents (water, methanol, ethanol, and dimethylformamide) has been thoroughly investigated [162]. Experiments have been performed on the electrolysis of oenanthic acid solutions and pure oenanthic acid, solutions of phenylacetic and phenoxyacetic acids, and also methyl and ethyl succinates on soft and hard graphite, vitreous carbon, and baked carbon electrodes. The Kolbe reaction proceeds in protic solvents on vitreous and baked carbon, while side reactions mainly occur on soft graphite (alkyl oenanthates are the main products in oenanthic acid solutions). Considerable differences were observed when pyrolytic graphite anodes with the surface parallel and at right angles to the plane of the lattice unit cells were used; in the former case the yield of products was appreciably lower. The above experiments appear to confirm the necessity to take into account the role of the adsorption stages also in anodic reactions on graphite materials.

This view is supported by the results of studies of other oxidation reactions on carbon anodes [163]. The authors postulate that, in accordance with Balandin's multiplet theory, the efficiency of the electrochemical oxidation is determined by the structural and energy correspondence between the substrate molecule and the electrode surface.

Despite the fact that Kolbe type anodic condensation reactions have already been studied for a long time and particularly vigorously in the last five–eight years, many problems involving their mechanism have still not been unambiguously solved and have been the subject of a lively discussion in papers by Conway, Eberson, Fioshin, and many other workers [1–3,69,154,156]. Since the kinetic aspects of the reaction based on an analysis of the literature up to 1967 have been summarised in an extensive review [69], we shall not consider here these problems in detail. We shall only note that analysis of numerous experimental data obtained in recent years using a number of electrochemical, radiochemical, and optical methods for the indentification of products of potentiostatic electrolysis and also the interpretation of these results in original studies lead (with rare exceptions [165,166]) to the following mechanisms of the processes corresponding to different sections of the polarisation curve (Fig. 3) in carboxylate solutions on platinum: section I—evolution of oxygen on a surface partly coated by the first form of the oxide and by adsorbed carboxylate ions; section II—ditto on a surface coated by a monolayer of the first form of the oxide and onset of the formation of the second form. Along section III, the discharge of anions begins, with formation of acyloxy- and alkyl-radicals adsorbed on platinum and displacing oxygen (mainly the second form). The high adsorption energy prevents their surface mobility and recombination. The transition region IV corresponds to the reorganisation of the surface oxide with the coadsorbed radicals, resembling the surface "two-dimensional crystallisation", which has been observed in solutions of inorganic acids [168]. Section V corresponds to the discharge of carboxylate ions on this modified surface with formation of condensation products via an electrochemical desorption mechanism.

Other views on the mechanisms of anodic processes in the oxidation of carboxylic acids have been developed in a study by Fioshin and Vasil'ev [82], where it was assumed that the discharge of carboxylate anions begins only at potentials corresponding to section V, i.e. when $\varphi \geqslant \varphi_{cr}$¶, while the inhibition of the oxidation in the transition region is caused by the specific features of the adsorption of these anions. This view, which has been supported by other workers [77,155], has been criticised in a review by Vijh and Conway [69].

¶ φ_{cr} is the initial potential on section V.

The results published in a number of communications[78,167,169,170] can serve as an additional argument in support of the above scheme, postulating the discharge of $RCOO^-$ under the conditions corresponding to the lower sections of the $i-\varphi$ curves. At potentials corresponding to section III the formation of alcohols and of a small amount of dimers was observed in the oxidation of pelargonic acid at a platinum anode in an alkaline medium[78,167], while in the electrolysis of ω-chloroacids in the presence of 1,3-dienes the formation of additive dimers was also noted[170]. The study of the electrochemical oxidation of propionate in an aqueous medium by the pulse and voltage-current methods also indicates the adsorption of the carboxylate up to φ_{cr}.[172] According to the authors, the rate-limiting stage is in the oxidation of $C_2H_5COO^-$; the adsorbed propionyloxy-radical formed decomposes into CO_2 and $C_2H_5^{\cdot}$, the latter reacting with $C_2H_5COO^{\cdot}$ to form ethylene and propionic acid. According to Takeda et al.[160] the charge transfer in the rate-limiting stage in glacial acetic acid on platinum, palladium, gold, lead dioxide, and graphite electrodes takes place via a layer of adsorbed $CH_3^{\cdot}$ or $CH_3COO^{\cdot}$ radicals.

Among the unsolved problems concerning the mechanism of the Kolbe reaction, that of the so called "anomalous" carboxylates occupies an important place. They include aromatic, substituted, and unsaturated carboxylic acids with multiple bonds and substituents X (X = halogen, OH, NH_2, Ph, or RCH=CH) in the α- and β-positions with respect to the carboxy-group. These compounds either do not undergo the dimerisation reaction at all or a dimer is formed in an insignificant yield,which appreciably limits the preparative scope of the Kolbe electrochemical synthesis. For example, in the anodic oxidation of acids of the adamantane series in an alcoholic medium[171] the main electrolysis product is the corresponding alkoxy-derivatives and not the dimers.

On the other hand, when the carboxy-group is linked to the bridgehead carbon atom via a methylene group, then electrochemical oxidation leads to ring expansion. The latter reaction can serve as a new method for the preparation of cyclic compounds with large rings.

The formation of a methoxy-derivative together with the dimer was observed by Coleman and Eberson[173] in the anodic oxidation of caesium 9-methylanthracene-10-acetate in a mixture of methanol and tetrahydrofuran. In a reaction involving the anodic decarboxylation of sodium epoxy-β-phenyl propionate at a platinum anode Japanese investigators[160] failed to detect the corresponding dimer; the main reaction products were benzaldehyde, acetophenone, benzyl acetate, and methyl benzoate. The desired product of the Kolbe electrochemical synthesis was not found (or was obtained in a negligible yield) also in the electrolysis of 2,2-dichloro-3-phenylcyclopropanecarboxylic acid on platinum in hydroxylated solvents[174], in the oxidation of cyclohexene-3-carboxylic acid and norborn-5-ene-2-carboxylic acid in acetonitrile[175], of 2-methoxy-1-cyclopentene-1-carboxylic acids in methanol[169], and of α-chloro- and α-fluoro-acids (valeric, caproic, and isobutyric)[176].

It has been shown[177,178] that, under the usual conditions of the Kolbe reaction, the electrolysis of aqueous solutions of perfluoro-acids also does not yield the dimeric product. In the electrochemical oxidation of trifluoroacetate at an oxidised platinum anode in the presence of added water, Na_2HPO_4, and H_2SO_4 in the electrolyte Knunyants and coworkers[179] obtained CF_3OOCF_3 and CF_3OCF_3 instead of hexafluoroethane. The results of Korchinskii and Andreev[180] confirm the fact that dicarboxylic acids also do not give rise to the corresponding dimers. In the oxidation of maleic and fumaric acids in the potential range corresponding to the upper section of the polarisation curve they observed the formation of acetylene. In a study[185] of the products of the preparative electrolysis of tri-t-butylcyclobutenedicarboxylic acid it was shown that, depending on the composition of the solution, various substances are obtained (2,3,5-tri-t-butylfuran, etc.), but the Kolbe dimer was not identified.

According to the majority of the investigators of these reactions (Eberson, Woolford, Fleischmann, etc.[1-3]), the anomalous behaviour of substituted carboxylates is associated with a lower ionisation potential of the radicals formed and their subsequent oxidation to the corresponding carbonium ions which then react with the nucleophilic components of the solution Z^- [reaction (1b)]:

$$RCOO^- \xrightarrow{-e,-CO_2} R^{\cdot} \begin{cases} \longrightarrow RR & (1a) \\ \xrightarrow{-e} R^+ \xrightarrow{Z^-} RZ\,. & (1b) \end{cases}$$

This view is shared also by the authors of the communication[171] concerning the adamantane acids. The results of the preparative electrolysis of phenylacetic acids[181] and also the study of the "pseudo-Kolbe reaction" mentioned above[173] lead to the same conclusion; in the latter case the authors concluded on the basis of voltage–current measurements that the electron is removed from the aromatic ring and not from the carboxy-group.

The occurrence of the substitution reaction with formation of the products RZ is favoured by the following conditions: low current densities, the use of graphite materials for the anode and of water as the solvent, pH > 10, and the addition of extraneous anions (HCO_3^-, HSO_4^-, $H_3PO_4^-$, Hal^-) and cations (Fe^{2+}, Mn^{2+}, Pb^{2+}, etc.). RZ can be formed either via a carbonium ion [reaction (1b)] or via the homolytic addition of R$^{\cdot}$ and Z$^{\cdot}$. It is usually difficult to differentiate the two reaction pathways. The so called "method of detecting radicals by an acceptor" is extremely effective in many cases for this purpose; its characteristics and examples of its practical application have been described[3,62].

Berenblit, Sokolov, and coworkers, who made a thorough study of the main products and by-products of the direct anodic condensation and cross-condensation of β-perfluoromethoxypropionic acid and certain monoesters of perfluorodicarboxylic acids in non-aqueous media, also concluded that the nature of the by-products cannot be accounted for solely by the homolytic interaction of the intermediate perfluoroalkyl radicals and requires the assumption of their simultaneous oxidation to the corresponding perfluorocarbonium ions[182,183].

On the basis of the mechanism described above for anodic processes in the oxidation of carboxylates, the ratio of the rates of reactions (1a) and (1b) will presumably depend, other conditions being equal, on the strength of the bond between the surface and the adsorbed RCOO$^{\cdot}$ (R$^{\cdot}$) radicals. In view of these considerations, a study was undertaken[17,18,184] of the electrochemical oxidation of carboxylates which are known not to from dimers (monoesters of $\alpha\beta$-unsaturated aliphatic dicarboxylic, aromatic, and alicyclic acids) in the presence of small amounts of vigorously adsorbed additives (for example unsaturated hydrocarbons, conjugated dienes, etc.). Indeed, under these conditions the heterogeneous-catalytic influence of such compounds on the dimerisation process was observed and the Kolbe reaction was achieved with an acceptable yield. In particular, in the oxidation of monomethyl maleate the product is the dimethyl ester of muconic

acid—the starting material for the synthesis of high-quality polymeric materials; the chemical methods developed for the synthesis of muconic acid are still insufficiently effective. Dimeric products were obtained also for other classes of anomalous carboxylates. There is a close relation between the adsorbability of the catalytic additive and its influence on the mode of the process—there is a direct correlation between the adsorption criteria and the yield of the dimer.

A similar effect is apparently encountered also in the case of perfluorocarboxylic acids, which are oxidised with formation of Kolbe products only in non-aqueous media, particularly those containing acetonitrile. The modification of the surface layer occurring in the adsorption of acetonitrile molecules in carboxylate solutions [186] probably leads to a weakening of the metal–adsorbate bond and to a change in the relative rates of reactions (1a) and (1b) in favour of the former, which increases. These considerations are supported by results [177,182,187], which confirm the influence of the solvent on the effectiveness of the dimerisation, including "cross dimerisation". In the latter case 1,1,1-trideuterotrifluoroethane and 1,1,1-trideuteropentafluoropropane were synthesised [187] in the electrolysis of mixtures of deuterated acetate with trifluoroacetic and pentafluoropropionic acids respectively by regulating the composition of the solution.

Anodic dimerisation reactions of the non-condensation type occur in the electrochemical oxidation of certain aromatic hydrocarbons, amines, phenols, and olefins. According to the ideas developed previously [188], the reactions can proceed via two mechanisms: ECC_N [reaction (2a)] and ECC_B [reaction (2b)], where the subscripts N and B denote respectively nucleophilic and electrophilic reaction stages:

$$2\,RH \xrightarrow{-2e} 2\,RH^{+} \rightarrow {}^{+}HRRH^{+} \begin{cases} \xrightarrow[X_N]{2Z^-} ZHRRHZ & (2a) \\ \xrightarrow{-2H^+} RR\,. & (2b) \end{cases}$$

(E) (C) (C_B)

Either dehydropolymers [reaction (2b)] or (in the presence of a suitable nucleophilic agent Z^-) disubstituted dimers [reaction (2a)] are formed under these conditions. The first pathway reduces in fact to an addition reaction, permits a different interpretation of the mechanism (via a homolytic addition stage), and will be discussed in the next Section. Some examples of reactions of this kind were described previously [189–191], but only the studies in recent years have shown that dimerisation of this type can serve as an effective method for preparative synthesis. In many instances nearly quantitative yields of the desired products were obtained.

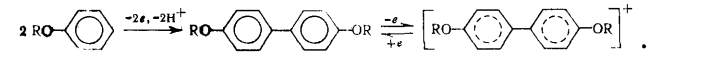
The electrolysis of benzene leads to a mixture of oligomers [192,193] with a yield reaching $A = 90\%$ in a solution containing $AlCl_3$ and HCl; [193] the electrochemical oxidation of 1,2,4-trimethoxybenzene and tetraphenylethylene resulted in the formation of 2,4,5,2′,4′,5′-hexamethoxybiphenyl ($A = 85\%$) [191] and 8,10-diphenylphenanthrene ($A = 100\%$) [194] respectively. The anodic dimerisation of many substituted anilines and phenols and also the mixed dimerisation of certain compounds have been achieved similarly.

The most important examples of these reactions have been compiled [1]. In recent years a series of studies on these lines was undertaken by Nyberg [195–197], who put forward an interesting concept to account for the mechanisms of the direct and mixed dimerisation of aromatic hydrocarbons. According to this concept, the higher the spin density or the positive charge density in the radical-cation formed, the greater the ease of its formation. It is thus possible to explain the preferential formation of biphenyls compared with diphenylmethanes and also the dependence of the yield of products on the concentration of the initial hydrocarbons in the anodic oxidation of polymethylbenzenes in non-nucleophilic media (CH_3NO_2 and CH_2Cl_2). [196] If the spin density (and the positive charge density) is higher in the ring of the radical-cation, biphenyls are mainly formed. On the other hand, if the spin density is higher in the substituent, then the benzylmethyl radical-cation with the charge located in the methyl group is formed preferentially; this radical-cation loses a proton and is converted into a benzyl radical, which is rapidly oxidised to a benzyl cation. The latter reacts with the initial hydrocarbon, giving rise to a diphenylmethane derivative:

$$ArCH_3 \xrightarrow{-e} ArCH_3^{+} \xrightarrow{-H^+} ArCH_2^{\cdot} \xrightarrow{-e} ArCH_2^{+} \xrightarrow{ArCH_3,\,-H^+} ArCH_2ArCH_3\,.$$

This view makes it possible to explain, for example, the formation of 1-mesitylnaphthalene in the absence of bimesityl in the mixed anodic dimerisation of naphthalene and mesitylene on platinum [196]. According to the above considerations, the more readily formed naphthyl radical-cation either dimerises in accordance with Eqn. (2b) to binaphthyl or interacts with mesitylene to form a mixed dimer; the absence of bimesityl confirms the fact that the corresponding mesityl radical-cation is not formed under these conditions.

The anodic dimerisation of a number of aryl esters derived from anisole, *o*-bromoanisole, and *o*-methylanisole has been achieved in high yields [198,199] by using trifluoroacetic acid or its mixtures with methylene chloride as solvents. Under these conditions, the dimeric radical-cation is stabilised and can be detected by the voltage–current procedure. According to the authors [198], the reaction proceeds as follows:



The dimerisation takes place only in the *p*-position and if the latter is blocked the radical-cation cannot be detected.

An interesting example of an effective combination of anodic and cathodic dimerisation in the same electrolyser has been described [200]. By electrolysing a solution of diethyl malonate and methyl acrylate in acetonitrile in the presence of potassium iodide under conditions favouring anodic dimerisation (high dilution, low current densities), the authors obtained high yields of the ester $(C_2H_5OOC)_2$–CH–$HC(COOC_2H_5)_2$ on the anode and dimethyl adipate on the cathode. The use of $LiClO_4$ instead of KI almost completely suppresses the formation of tetraethoxycarbonylethane but does not effect the yield of dimethyl adipate. The dimerisation of acetoacetic ester also does not occur in the presence of ClO_4^-—the product is 2-ethoxycarbonyl-4-methoxycarbonyl-1-methylfuran.

In other cases the anodic dimerisation of anionic dicarbonyl compounds such as sodium dialkylmalonate and sodium acetylacetonate was achieved successfully with satisfactory yields [201–203]. A large number of examples of the anodic dimerisation of the anions of polar organic compounds have been described:

$$2\,R^{-\delta}\!-\!X^{+\delta} \xrightarrow{-2e;\,-nX^+} 2R^{\cdot} \rightarrow RR,$$

in particular phenols, oximes, aliphatic nitrocompounds, organometallic compounds, alkynes (see Eberson and

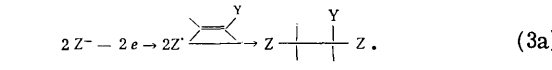
Schäfer[1], Table 12), and also enolic ethers[204]. In certain cases a mixed dimerisation can be achieved with a high degree of efficiency[205].

V. ANODIC ADDITION REACTIONS

This class of reactions, which has been vigorously investigated in the last decade, probably involves the greatest concentration of the advantages of electrochemical methods formulated above. Processes of this type are in many cases distinguished by a high efficiency, selectivity, and ease of the synthesis of relatively high-molecular-weight compounds from simple monomers.

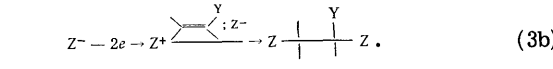
According to modern ideas, it is possible to achieve three versions of the anodic addition of a nucleophilic agent to the double bonds of the acceptor.

(a) Via a radical generated on the anode:



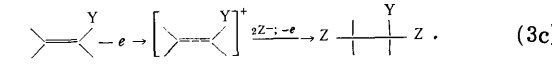
(3a)

(b) Via the electrophilic agent formed initially:



(3b)

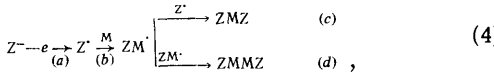
(c) Via the radical-cation formation stage:



(3c)

These reaction pathways can be by no means always distinguished; the criteria proposed are as a rule insufficiently reliable[1-3].

The radical pathway is assumed by the majority of investigators for the electrochemical additive dimerisation of olefins initiated by the electrochemical oxidation of carboxylic acids, alcohols, water, and nitric acid[206-238]:



(4)

where M is the olefin molecule and Z = RCOO, $H_2C_2O_4$,[15, 206,211-216,223,224,227] RO,[217-221] halogen[226], (CH_3CO_n).$CH_{n=1,2}$,[10,230-232] $O_2NC_nH_{2n-2}$,[234,235] N_3,[237] etc.[197,236] Among unsaturated compounds, mainly conjugated dienes[15,52,206-227], styrene[229,234-236], and ethyl vinyl ether[230,234,235] as well as other activated olefins, are involved in this reaction. The dimerisation reactions of Z as well as the homolytic abstraction of hydrogen from the electrolyte components ($Z^{\cdot} + RH \rightarrow HZ + R^{\cdot}$) take place simultaneously with reaction (4). When $Z^- = AlkCOO^-$, stage (4a) is followed by the spontaneous decarboxylation stage, but, when $Z^- = ArCOO^-$, this does not occur, because of the much greater stability of the aroyloxy-radicals compared with acyloxy-radicals. Certain substituted boronic acids behave similarly to aliphatic carboxylates[232].

The interpretation of the mechanism of the anodic additive dimerisation in accordance with Scheme (4) has not been altogether generally accepted. For variants of the reaction in which $Z^- = AlkO^-$, $ArCOO^-$, and certain other species, heterolytic pathways are assumed in a number of investigations, postulating a preliminary oxidation of the substrate on the anode followed by the interaction of the resulting carbonium ions by Z^-. A number of reports are devoted to the mechanism of reactions of this type[1-3].

The accumulated experimental data for this field were recently analysed and the possible reaction pathways were discussed in relation to the additive dimerisation initiated by the oxidation of carboxylates[3] and alcohols[7]. The study of the influence of various factors on the mode and efficiency of additive dimerisation has shown that, regardless of the nature of Z^- ($HC_2O_4^-$, $C_nH_{2n-2}COO^-$, $AlkOOCArCOO^-$, ω-ClC_nH_{2n-2}.COO^-, and $AlkO^-$[62,206-215]), the fundamental kinetic characteristics are similar. This apparently indicates a common mechanism for such processes. The homolytic mechanism of the addition reaction is unambiguously indicated by the nature of the products obtained in certain variants of the additive dimerisation, for example that initiated by alkyl radicals formed in the electrochemical oxidation of carboxylates[206-209,223,224]. In some investigations experiments on potentiostatic electrolysis showed that the additive dimers are formed at potentials lower than those required for the oxidation of substrate molecules[170].

Analysis of the results of studies of the additive dimerisation reactions has shown that the necessary condition for their occurrence is the adsorption of acceptor molecules on the electrodes.

High yields of adducts were obtained using as acceptors compounds for which an appreciable adsorption activity has either been found or postulated (on the grounds of structural considerations) at the high positive potentials required for the formation of $RCOO^{\cdot}_{ads}$. This is also indicated by the following considerations. Whereas the formation of $R^{\cdot}$ in the bulk of the solution[165,166] is in principle possible for unsubstituted straight-chain carboxylates (this is particularly likely for phenylacetic acids[19]), such a reaction is probably ruled out in the oxidation of "anomalous" carboxylic acids, which are not dimerised. The products formed indicate the oxidation of $R^{\cdot}$ to the corresponding carbonium ion. Such radicals can therefore be formed only in the adsorbed state and the formation of additive dimers in these instances constitutes convincing evidence for the involvement of the substrate also in the adsorbed form. In the studies quoted previously[17,18,184,225] the above phenomenon was confirmed for non-dimerising carboxylates of various classes in the presence of an adsorbable acceptor (adsorption has been demonstrated by independent methods[35,55,56,116,134]). As a result of the reaction, appreciable amounts of polymeric products were obtained only under special conditions (at extremely low current densities); chain termination at stages where $m \leq 2$ (m is degree of polymerisation) also indicates a heterogeneous process. The transfer of $R^{\cdot}$ to the bulk of the solution (which usually contains high acceptor concentrations) would inevitably lead to the appearance of at least oligomers in consequence of the "cage effect".

It follows from the foregoing considerations that similar reactions involving suitable acceptors, for example 1,3-dienes, can serve as an effective method for the detection of the intermediates formed during electrolysis.

Elementary kinetic analysis of the reaction mechanisms involving adsorbed acceptor molecules on the electrode demonstrates a satisfactory agreement between the variations of the yields of individual adducts with a number of process parameters[238]. It follows from Eqns.(4a), (4b), (4c), and (4d) that the relative rates of formation of the reaction products must be extremely sensitive to changes in the effective concentrations of $R^{\cdot}$, which is determined, other conditions being equal, by the anodic current density, and to the degree of surface coverage by the olefin. Indeed, it has been frequently shown that, by altering the anodic current density, the nature of the electrode

material, and the acceptor concentration, it is possible to vary within wide limits the ratios of the products formed and to carry out the process under conditions favouring the synthesis of each separately [208-221]. This factor converts the reaction into a unique method of synthesising many valuable polyfunctional compounds.

The mechanism of addition via an anodically generated electrophilic agent is apparently assumed only for oxidative halogenation at double bonds and also for the electrochemical analogue of the Ritter reaction, achieved by Foita et al. for cyclohexene [239] and then by Weinberg and Hoffmann [240] for other compounds on chlorination in acetonitrile. In the former case chlorination of cyclohexene yielded 2-acetamido-1-chlorocyclohexane, while in the latter electrochemical halogenation of 1-phenylbut-2-ene and cyclopentene also led to 2-acetamido-1-halogeno-adducts. The introduction of acetamido-groups likewise takes place in the electrochemical oxidation of α-substituted and aromatic carboxylic acids [241,242], adamantane, 1-halogenoadamantanes and esters [243,244] in nitriles. According to the ideas of Eberson and Nyberg [241], the electrochemical introduction of acetamido-groups into carboxylates proceeds via the intermediate formation, as a result of two-electron oxidation of a carbonium ion, which reacts further with acetonitrile in the following way:

$$R_3CCOO^- \xrightarrow{-2e,-CO_2} R_3C^+ \xrightarrow{CH_3CN} R_3CN{=}\overset{+}{C}CH_3 \xrightarrow{H_2O,-H^+} R_3CNHCOCH_3 \quad (5a)$$

Similar views on the reaction mechanism have been expressed by other workers [243,244]. However, Japanese investigators, who studied the oxidation of benzoic acid in acetonitrile and propionitrile [242], suggest that the addition products (*N*-acetylanthranilic and *N*-propionylanthranilic acids) are formed via the oxidation of the benzoate ion to the benzoyloxy-radical, which is deprotonated and reacts further with the nitrile.

A number of studies on the anodic chlorination of ethylene [245], vinyl chloride, and butadiene [246] in an aqueous medium and in aliphatic alcohols have been published in recent years. In the case of ethylene dichloroethane was obtained under optimal conditions in an aqueous medium in yields up to 80%, while in the oxidation of olefins in a hydrochloric acid solution in methanol mixed chloro-methoxy-adducts were formed together with chloro-derivatives. Comparison of the electrochemical and chemical chlorination of ethylene (the influence of the nature of the anode, of admixtures in HCl, and other factors) demonstrated definite differences between the mechanisms of the two processes and led the authors [245] to the conclusion that adsorption processes play a significant role in the electrochemical reaction.

The third variant of the anodic addition reaction presupposes a two-electron transition in stages, initiated by the oxidation of the substrate molecule itself (an olefin or an aromatic compound). The addition products are formed in accordance with an EC_BEC_B mechanism:

$$\underset{(E)}{M} \xrightarrow{-e} \underset{(C_B)}{M^+} \xrightarrow{Z^-} \underset{(E)}{ZM^\cdot} \xrightarrow{-e} \underset{(C_B)}{ZM^+} \xrightarrow{Z^-} ZMZ \quad . \quad (5b)$$

This pathway has been postulated by some investigators for the alkoxylation and acetoxylation of furan derivatives, quinones, and substituted pyridines [7]. The anodic depolarisation effect, observed in many instances when the substrate is introduced into the electrolyte, has been frequently used as a criterion of the occurrence of the process via this mechanism. Critical comments have often been made concerning this approach [2,3,62].

VI. SUBSTITUTION REACTIONS

The study of anodic substitution reactions has also attracted much attention in recent years, since processes of this type give rise to a wide variety of synthetic possibilities. Studies in this field have been reviewed [1,247,248]. Here we shall deal only with certain general considerations concerning reactions of this kind.

Processes in which a group X (usually a hydrogen atom) in the substrate molecule RX is replaced on electrochemical oxidation by a substituent Z (Z = OR, OCOR, halogen, CN, etc.) belong to this class. The reactions can be divided into three groups in accordance with their mechanism [1].

(a) Homolytic substitution of hydrogen by a radical generated on the electrode:

$$Z^- \xrightarrow{-e} Z^\cdot \xrightarrow{RX,-XZ} R^\cdot \xrightarrow{Z^\cdot} RZ \quad . \quad (6a)$$

(b) Substitution of the condensation type in the electrolysis of carboxylates:

$$RCOO^- + Z^- \xrightarrow{-2e,-CO_2} RZ \quad . \quad (6b)$$

(c) Nucleophilic substitution via a radical-cation:

$$RX \xrightarrow{-e} RX^+ \xrightarrow{Z^-} RXZ^\cdot \xrightarrow{-e,-X} RZ \quad . \quad (6c)$$

As for anodic addition reactions, it is frequently difficult to distinguish the substitution processes involving different mechanisms.

The most striking examples of the first type are apparently those involving electrochemical halogenation. Among these, anodic fluorination is of the greatest practical importance. It constitutes a convenient method for the synthesis of perfluoro-compounds and has a number of advantages over the analogous chemical reactions, obviating the necessity for working with elemental fluorine [5,6,249-252].

The radical mechanism of the electrochemical fluorination proposed by Simons [250] is not, however, generally accepted at present. This reaction exhibits a high electrocatalytic specificity and proceeds in liquid hydrogen fluoride, mainly on nickel anodes. In an early study by Gramstad and Haszeldine [251] it was suggested that the active principle in this reaction is higher nickel fluorides. Subsequently a similar view was developed in another investigation [252]; the authors believe that many kinetic features of the reaction (for example the induction period) agree well with the hypothesis of the intermediate formation of complexes by the organic substance and nickel fluorides, such as $(RH_2)_2NiF_6$ and $(RH)_3NiF_6$.

The influence of the preliminary treatment of the electrodes on the electrochemical fluorination process has been established [253]. In particular, the induction period is shortened for nickel anodes coated chemically by NiF_2. The authors base their treatment on the mechanism of the anodic fluorination of organic compounds involving the initial formation of their complexes with nickel fluoride followed by electrochemical oxidation at the C–H bond with formation of radicals, which recombine with F$^\cdot$. In a study of the fluorination of aliphatic amines by Japanese workers [256], a mechanism was proposed for the electrode processes involving the discharge of F^-, the homolytic substitution of H by F, and oxidative cleavage of the C–C and C–N bonds followed by polymerisation.

On the basis of the results of the anodic fluorination of fluorobenzenes on platinum in acetonitrile [255], Knunyants and coworkers concluded that in this case the first stage of the process is one-electron oxidation of the substrate followed by the interaction of the radical-cation with a fluoride anion; the second stage is accompanied by the simultaneous transfer of a second electron with abstraction of a proton.

Thus the mechanism of the anodic fluorination is still controversial. Various hydrocarbons, including halogenohydrocarbons, carboxylic acids, ethers, amines, nitriles, and other classes of organic compounds have been used as the substrates in this reaction. Apart from the investigations the results of which are discussed in earlier reviews [1,5,6,247], mention should also be made of a number of recently published communications dealing with the fluorination of carbon monoxide, phosgene, substituted benzene and pyridine [259,260], methane, propane, ethylene [254], fluorobenzene and trifluoromethylbenzene [255], amines [256,257], tetrahydrofuran [261], ethylene chlorohydrin [262], dithiols and cyclic sulphides [263], *NN*-dialkylanilines and *NN*-dimethyltoluidines [264], ethylene glycol ethers [265], chloroethers [266], and other compounds [258].

In all cases a complex mixture of fluoro- and perfluoroderivatives, including degradation products and polymers (their amount is particularly large in the fluorination of alcohols and amines), is usually formed. The highest selectivity has apparently been achieved in a study [265] of the fluorination of triphenylmethane; under the conditions discovered in that investigation, fluorotriphenylmethane is formed in 80% yield.

Under the conditions of electrochemical fluorination, carboxylic acids do not undergo anodic condensation, but give rise to a mixture of substitution products with different fluorine contents in the molecule of the initial acid; the yields of the fluoro-derivatives increase with the molecular weight of the homologues. It has been shown [267,268] that the presence of alkoxy-groups in the carboxylic acid greatly facilitates the fluorination reaction compared with the unsubstituted analogues. The yields of perfluoromethoxyacyl fluorides are significantly higher than in the fluorination of the corresponding acids (14–41%); with increase of the chain length of the alkoxy-group, its stability in the electrochemical fluorination processes falls appreciably. The organic solvents usually employed in anodic reactions are not inert under the fluorination conditions, in particular acetonitrile gives rise to monofluoroacetonitrile and to succinodinitrile.

The homolytic mechanism has been adopted in most investigations for other halogenation reactions. However, these problems have been studied in much less detail than fluorination because they can be achieved without significant difficulties by the usual chemical methods. Several communications dealing with the behaviour of various electrodes (platinum, iridium, and ruthenium) in chloride solutions and also with the electrochemical chlorination of simple aliphatic hydrocarbons on graphite, platinum, and iridium anodes were published recently [269-271]. It has been shown [269] by the potentiodynamic method that the adsorption of Cl^- on platinum begins at hydrogen desorption potentials; it is postulated that Cl˙ atoms are adsorbed on a $Cl\bar{a}ds$ layer. Cl^- ions are not adsorbed on iridium anodes at Cl_2 and O_2 evolution potentials. Experiments on the electrochemical chlorination of methane, ethane, and ethyiene in the dark and under illumination led Kuhn and coworkers [270] to the conclusion that the substituion process has no specific heterogeneous features and is the result of a photochemically or thermally initiated reaction of the organic substance with molecular chlorine. This mechanism makes it possible to explain the observed higher rate of reaction compared with the value calculated on the basis of diffusion kinetics. According to the authors, the depolarising influence of the test gases is caused by the decrease of the concentration of Cl_2 evolved at the anode.

On the other hand, the results of the anodic chlorination of ethane on a graphite electrode, where a mixture of dichloroethane (75%) and ethyl chloride (20%) is formed, differ significantly from those obtained in chemical chlorination with molecular chlorine, which apparently indicates a heterogeneous mechanism of the reaction under these conditions [272]. Mastrogostino et al. [273], who carried out the electrochemical chlorination of aromatic hydrocarbons (benzene, toluene, and xylene) in anhydrous acetic acid at chlorine oxidation potentials, concluded that in this case the chlorinating agent is Cl_2^- and not Cl˙.

The radical substitution pathway has been adopted for the alkoxylation and acetoxylation of organosilicon compounds [274,275] and substituted amides [276]. However, Eberson and Nyberg [277] assume for this reaction the pathway corresponding to the third case, which is discussed in detail below. Substitution reactions accompanying the electrolysis of carboxylates have already been mentioned in the appropriate Section. Conditions favouring this reaction and hindering dimerisation are low current densities, high temperatures, water as the solvent, the addition of extraneous inorganic anions and cations, pH > 10, and graphite and non-platinum metal anodes. The preferential formation of substituted products is observed in the electrochemical oxidation of "anomalous" carboxylates (Section IV). Alcohols are formed in an alkaline medium (the Hofer–Moest reaction; $Z = OH^-$).

It is extremely difficult to decide unambiguously whether there is substitution via a carbonium ion R^+ or whether mixed radical recombination of R˙ with Z˙ takes place. In many instances the products RZ formed in electrolysis (ethers, esters, and alcohols) have a structure typical for heterolytic substitution involving a carbonium ion [278]. Sometimes the nature of the substances formed in the electrolysis can be more readily accounted for by postulating the formation of an intermediate alkoxonium ion $RCOO^+$, which then either combines with Z^- or undergoes solvolysis [279-281].

The substitution reactions occurring in the electrolysis of carboxylates have been used successfully to synthesise alcohols, acetamides, nitro- and alkoxy-derivatives, and many other classes of organic compounds [1,248]. The necessity for the preliminary substrate oxidation stage has been assumed by the majority of the investigators of the substitution reactions of aromatic compounds. This conclusion is frequently justified by the depolarising influence of the substrate on the anode under galvanostatic conditions, although, as stated previously [2,3], such arguments are not always sufficiently convincing. This also applies to the interpretation of certain results of potentiostatic electrolysis. For example, the acetoxylation of aromatic substances at $\varphi < \varphi_{cr}$, which has been regarded [282-284] as an important confirmation of mechanism (6c), can be readily interpreted also as a result of homolytic interaction with a substrate molecule of the radical AcO adsorbed on the electrode below φ_{cr}.

A detailed comparison of the composition of the anodic substitution products of many aromatic compounds with the results of the analogous chemical reactions has shown, however, that in many instances pathway (6c) is preferable to the homolytic mechanism. In particular an $EC_N\bar{E}C_B$ mechanism has been adopted for the introduction of

acyloxy-, cyano-, and bromo-groups into the benzene ring or at the α-carbon atom in alkylamines:

$$\underset{(E)}{HArR} \xrightarrow{-e} \underset{(C_N)}{\overset{+}{H}ArR} \xrightarrow{Z^-} \underset{(E)}{ZHArR} \xrightarrow{-e} \underset{(C_B)}{ZH\overset{+}{A}rR} \xrightarrow{-H^+} ZArR \,. \qquad (7a)$$

The substitution in the side chain is best explained by an EC_BEC_N mechanism [285-288]:

$$\underset{(E)}{ArCH_2R} \xrightarrow{-e} \underset{(C_B)}{Ar\overset{+}{C}H_2R} \xrightarrow{-H^+} \underset{(E)}{ArCHR} \xrightarrow{-e} \underset{(C_N)}{Ar\overset{+}{C}HR} \xrightarrow{Z^-} ArCHZR \,. \qquad (7b)$$

The anodic substitution reactions constitute in many cases convenient and effective methods for the synthesis of a wide variety of compounds and are frequently a useful alternative to purely chemical methods. In addition to earlier studies in this field, discussed previously [1-3,248], mention should also be made of certain investigations in recent years. In particular, Japanese workers [289] achieved the electrolytic benzoyloxylation of a number of *NN*-dimethylamides in the oxidation of benzoic acid in organic solvents and demonstrated a significant influence of the nature of the solvent and of the supporting electrolyte on the yield of products. The maximum yields were achieved in acetonitrile in the presence of $(Et_4N)ClO_4$. An appreciable role of solution composition has also been noted for reactions involving the introduction of hydroxy- and acetamido-groups [290] and also in the methoxylation of alkylbenzenes [291] and in the acetoxylation of propene [301]. In a study [292] of the anodic introduction of bromo- and cyano-groups into *p*-dimethoxybenzene and 9-phenylanthracene in acetonitrile by the volt-amperometric method and the method based on a rotating electrode with a ring it was possible, according to the authors, to refine the mechanism of the anodic substitution of aromatic compounds. It was concluded that the interaction with the nucleophilic agent proceeds at the stage involving the formation of an aromatic radical-cation and not after the formation of a carbonium ion. In another report the results of the introduction of cyano-groups into substituted diphenylamines are considered [293]. The reaction with *o*- and *m*-derivatives takes place only at the *p*-position and the yield is high (44–61%). It is suggested that the oxidation is accompanied by the formation of a radical-cation, which then interacts with CN^-. Comparison of the results obtained for the introduction of cyano- and acetoxy-groups into a number of aromatic hydrocarbons and their derivatives (biphenyl, toluene, chlorobenzene, anisole, naphthalene, and mesitylene) has shown that substitution by CN groups takes place almost exclusively in the *p*-position, in contrast to the acetyl group, which the authors explained by the more marked nucleophilic properties of the cyano-group [302]. Eberson and coworkers support a heterolytic mechanism for this reaction [302,303].

The formation of products of anodic substitution (Z^- = CH_3O^- or AcO^-) in the allyl position was established in a study of the oxidation of olefins in acetic acid, methanol, acetonitrile, and in an acetonitrile–water mixture at a carbon electrode [294]. To account for the results, the authors base their treatment on an ECEC mechanism. Nyberg and coworkers [295] succeeded in achieving the acetoxylation of a number of methylbenzenes in the side chain with a high yield and selectivity. The results were interpreted from the standpoint of the above concept of positive charge and spin densities. In another study [296] aromatic hydrocarbons (mesitylene, naphthalene, and butylbenzene) were oxidised anodically in the presence of NO_3^-. It was established that in this case three types of substitution processes take place: hydroxylation, nitration, and nitrohydroxylation, the ratios of the products of these reactions depending on the concentration of the substrate, the potential, and the nature of the anode. Other variants of the anodic substitution reactions were also investigated: the introduction of the pyridyl group into substituted anthracenes [297] and hydroxylation of phenols [298-300]. It has been shown [274,275] that the electrochemical pathway is also extremely effective for the synthesis of methoxy- and acetoxy-derivatives of a number of organosilicon compounds.

In most of the earlier studies in this field the results were treated from the standpoint of homogeneous chemistry. However, many data obtained recently conflict with this approach.

Thus in a study of the electrolytic acetoxylation of indane by Eberson and coworkers [73,74] it was not possible to detect indene —the elimination product from the 1-indanyl cation, the formation of which was to be expected when an ECEC mechanism was postulated for reactions of this type. The nature of the products indicates further oxidation of indene, which is formed in the adsorbed state according to the authors. In another study [76], dealing with the anodic acetoxylation of 2-t-butylindan on platinum and PbO oxides, the authors obtained an anomalous ratio of the *cis*- and *trans*-isomers, compared with homogeneous reactions, and suggested that the adsorption partly controls the stereochemistry of this reaction. From the authors point of view, the influence of the addition of extraneous aromatic compounds (naphthalene and pentamethylbenzene) on the relative amounts of the *o*- and *p*-substituted derivatives obtained in the anodic acetoxylation of anisole is consistent with the conclusion that the substrate is adsorbed on the anode [75]. The effect is observed even at a very low concentration of the additive, tending to a limit with its increase. Certain compounds (biphenyl and t-butylbenzene) do not affect the relative amounts of the isomers, which is explained by their weak adsorbability under these conditions.

Regardless of the reliability of this type of procedure for the estimation of the degrees of adsorption of the electrolyte components on electrodes, the above results confirm the fruitfulness of the combined approach to the study of chemical reactions and surface phenomena for a more correct understanding of the mechanisms of reactions of the classes considered.

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The Low-temperature Quantum-mechanical Limit for the Rates of Chemical Reactions

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The influence of quantum-mechanical effects on one of the fundamental laws of chemical kinetics—the Arrhenius law—is considered. Criteria characterising the limits of the low-temperature region where the extent of quantum-mechanical tunnelling transitions exceeds exponentially the transitions over the barrier are quoted. Studies of the low-temperature tunnelling of electrons and hydrogen atoms are briefly mentioned and the history of research on low-temperature radiation-induced solid-phase polymerisation, the development of which led to the discovery of the phenomenon of the low-temperature quantum-mechanical limit for the rates of chemical reactions in relation to the formaldehyde polymerisation reaction, is briefly considered.

The results of experiments using low-inertia calorimeters, whereby it is possible to determine directly the average time (τ_0) required to add one new link to the polymer chain of formaldehyde during its polymerisation by radiation and during postpolymerisation and to establish that below 80 K the increase of τ_0 slows down and that at $T \approx 10$-4 K the time τ_0 reaches a plateau ($\tau_0 \approx 0.01$ s), are described. Possible explanations of the observed low-temperature limit for the rate of a chemical reaction are critically examined and a semiquantitative explanation is given for this phenomenon, which may be particularly common in combined electronic-confirmational transitions in complex biological molecules and may play a definite role in chemical and biological evolution (cold prehistory of life?).

The bibliography includes 56 references.

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I. INTRODUCTION

Little more than 100 years have elapsed since the discovery (1869) of the first quantitative law of chemical kinetics—Guldberg and Waage's law of mass action. The second fundamental kinetic law is 20 years more recent, having been discovered in 1889. Svante Arrhenius explained the marked temperature dependence of the rates of chemical reactions and derived his famous exponential formula, according to which the reaction rate constant k is proportional to e^{E/k_BT}, where E has since been called the activation energy (k_B is the Boltzmann constant).

It is of interest to recall certain aspects of the discovery of the Arrhenius law. The Swedish scientist investigated the inversion of cane sugar by acids in aqueous solution and suggested that sugar exists in two equilibrium forms, active and inactive, and that the equilibrium between these forms obeys the law of mass action. The rate of inversion is proportional to the concentration of the active form. Furthermore, Arrhenius believed that the rate of inversion is much lower than the rate of interconversion of the active and inactive forms of sugar, i.e. that the chemical reaction does not decrease the concentration of the active form relative to its equilibrium value, which is low in any case, and does not disturb the equilibrium between the active and inactive forms: $C_a/C = K$ (C_a is the concentration of active molecules and C that of inactive molecules). Then the rate of inversion of active sugar molecules is

$$-\frac{dC_a}{dt} \simeq -\frac{dC}{dt} = k_a C_a = k_a K C = kC, \quad (1)$$

where k_a is the actual rate constant and k the observed rate constant.

Arrhenius suggested that the rate constant for the inversion of active sugar molecules k_a is independent of temperature and that the increase of the observed rate of inversion with increasing temperature is wholly determined by the van't Hoff reaction isochore (derived from thermodynamic considerations five years earlier—in 1884):

$$\frac{d\ln k}{dT} = \frac{d\ln K}{dT} = \frac{Q}{k_B T^2}, \quad (2)$$

where Q is the energy required to convert an inactive sugar molecule into an active molecule.

Arrhenius's main idea has remained unchanged until our time. Admittedly Arrhenius assumed that the active form of the initial reactant consists of a chemical modification, whereas now we regard the active form as differing from the inactive form in having a higher energy content. However, the two approaches are by no means completely incompatible. On the contrary, the initial formulation of Arrhenius's idea was actually revived to some extent by the activated complex theory, which treats the rate of reaction on the basis of the equilibrium between the initial reactants and a transition state.

In one way or another we now define the activation energy as the difference between the average energy of the molecules entering into the chemical reaction and the average energy of all the initial molecules. In other words, the activation energy E can be defined as the height of the potential barrier which prevents the mutual approach of the reacting atoms and molecules.

Since the rate constant for a chemical reaction k is proportional to the fraction of reacting molecules with energy exceeding the activation energy E, the distribution of molecules in terms of the kinetic energy W, described by the Boltzmann equation (1868)

$$\frac{1}{N}\cdot\frac{dN}{dW} = \frac{2\pi}{(\pi k_B T)^{3/2}}\sqrt{W}\cdot e^{-\frac{W}{k_B T}}, \quad (3)$$

naturally leads to a temperature variation of the rate of reaction in accordance with the exponential Arrhenius law:

$$k = Ae^{-\frac{E}{k_B T}}. \quad (4)$$

The Arrhenius law has been confirmed by many thousands of examples over a wide range of temperatures and the activation energy has become one of the most important parameters subsequently employed in chemical kinetics.

Clearly, when many chemical reactions occur in a system, the observed temperature variation of the rate of the overall process may be more complex and may not be described by the Arrhenius law. This is illustrated by two examples in Fig. 1. Suppose that two reactions take place in the system: (1) A → B and (2) A → C with activation energies E_1 and E_2 and $E_2 > E_1$. If the formation of C in reaction *2* must be preceded by reaction *1* (for example, reaction *2* proceeds as follows: A + B → C + B), then an apparent increase of the activation energy for the formation of C will be observed as the temperature is reduced with a gradual transition from $E = E_1$ to $E = E_2$. The observed rate of appearance of C is in this case determined by the slower of the two reactions. On the other hand, if the reactions occur simultaneously, then a decrease of temperature entails an apparent decrease of the activation energy for the disappearance of A with a gradual transition from $E = E_2$ to $E = E_1$—the observed rate of decrease of the amount of A is determined by the faster of the two reactions and a decrease of temperature results in an "automatic" selection of the pathway leading to the transformation of A with the smallest activation energy. Looking ahead, we may note that the overall form of the temperature variation of k then resembles the variation obtained for a unique pathway with allowance for quantum-mechanical tunnel effects.

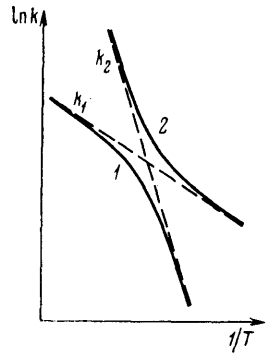

Figure 1. Characteristic temperature variation of the observed rate constant k for the disappearance of the initial reactants or for the appearance of the reaction products in two consecutive (curve *1*) and simultaneous (curve *2*) reactions with different activation energies ($E_2 > E_1$).

The introduction of quantum mechanics led to three most important consequences for chemical kinetics. Firstly, quantum mechanics explained the very presence of a potential barrier in chemical reactions. This barrier arises because electrons obey Fermi-Dirac statistics, i.e. the Pauli principle extends to them—the number of sites in each energy state is limited and for this reason exchange repulsion between electrons takes place. Secondly, when the problem of the excess energy of the reacting atoms and molecules is considered, one must consider in the general case the quantisation of the rotational, vibrational, and electronic forms of this

energy. Thirdly, and this is now the most important factor for our purposes, quantum mechanics led to the discovery of the possibility of various transitions not only over potential barriers but also through these barriers—the so called tunnelling transitions.

II. THE TUNNEL EFFECT IN CHEMICAL KINETICS (GENERAL POSTULATES)

The problem of the possible role of the tunnel effect in chemical kinetics was first formulated by Borgin[1] as early as 1929 and important contributions were made to the theoretical analysis of this problem by Roginskii and Rozenkevich's studies (1930)[2] and by the large series of studies by Bell, starting from 1933–1937.[3]

However, the attempts to observe experimentally the contribution of the tunnel effect at relatively high temperatures did not yield unambiguous results, while the region of low temperatures, where the tunnel effect should be manifested more clearly, remained uninvestigated for a long time. It was not until the 1950's that interest was aroused in the occurrence of all possible chemical reactions at low temperatures and the experimental observation of even very slow reactions of this type became possible (for example by microwave spectroscopy, by tracer atom techniques, etc.). In this connection the present author formulated in 1959 criteria characterising the limits of the low-temperature region where the tunnel effect exceeds Arrhenius transitions over the barriers and the kinetics of tunnelling transitions through symmetrical potential barriers were examined in general terms[4,5].

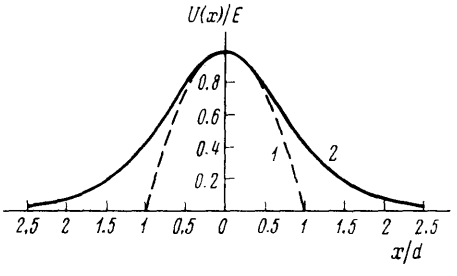

Figure 2. Typical examples of one-dimensional potential barriers: 1) parabolic; 2) Eckart.

Qualitative analysis of the temperature criteria is very simple. For a strong tunnel effect, one requires the "quantisation" of the system, i.e. its "quantum-mechanical size" λ must be greater than its classical size d. On the other hand, a low value of the ratio k_BT/E is needed in order that the transitions over the barrier should be slow. Therefore the following inequality must hold in order that the tunnel effect should predominate: $\lambda/d > k_BT/E$, or, in other words, $\hbar/d\sqrt{2mE} > k_BT/E$ or $T < (\hbar/k_Bd\sqrt{2})\sqrt{E/m}$, where E is the height of the barrier, d its half-width, and m the mass of the tunnelling species. An exact treatment yields an additional multiplier π, so that the temperature T_t below which tunnel effects predominate exponentially over Arrhenius effects is given by the following formula for any barrier described by a parabola at its apex:

$$T_t = \frac{\hbar}{k_B\pi d\sqrt{2}}\sqrt{\frac{E}{m}}. \qquad (5)$$

when $E \simeq 1$ eV and $d \simeq 3$ Å, $T_t \simeq 50$ K for protons and $T_t \simeq 1600$ K for electrons.

In the formulae describing the permeability of potential barriers, it is convenient to consider the characteristic energy of the system $\epsilon = \hbar^2/md^2$ and to compare two dimensionless parameters: E/ϵ and E/k_BT.

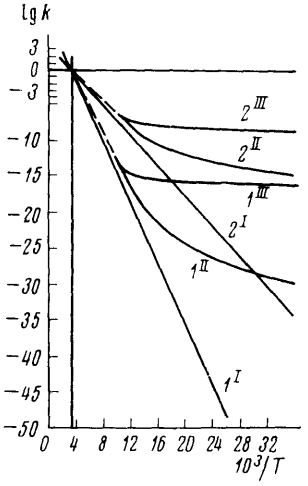

Figure 3. Temperature variation of the rates of reactions involving transitions over barriers (curves *1*II and *2*I) and with allowance for tunnelling through Eckart (curves *1*III and *2*II) or parabolic (curves *1*III and *2*III) barriers; barrier parameters: $a = 50$ (curves *1*) or $a = 25$ (curves *2*).

The typical forms of potential barriers are the parabolic barrier $U(x) = (1-x^2/d^2)E$ and the so called Eckart barrier $U(x) = ECh^{-2}x/d$ (Fig. 2). The dependence of lg k on $1/T$ with and without allowance for the tunnel effect is illustrated for both barriers in Fig. 3 with $a = \pi\sqrt{2}\sqrt{E/\epsilon} = 25$ and 50. At low temperatures ($T < T_t$) we have instead of the usual Arrhenius relation a unimolecular reaction rate constant which decreases as $T^{3/2}$ for the Eckart barrier tending towards zero, because the "bottom" of a barrier of this form is infinitely wide. On the other hand, in the case of the parabolic barrier the rate constant for a unimolecular chemical reaction reaches a plateau at low temperatures, tending to a definite limit.

A change from the continuous (Boltzmann) energy distribution to a discrete quantum-mechanical distribution of the tunnelling mass in a typical case of a symmetrical transition between systems, described by Morse potential curves (Fig. 4), does not alter the above criterion for the boundary temperature T_t of the "tunnelling region". For a quantum-mechanical distribution with respect to energy levels, the rate constant reaches a plateau at low temperatures, whatever the form of the barrier, which corresponds to a tunnelling transition from the zero-point vibrational level.

The picture described above is extremely simple but unfortunately has been used very rarely in this form. In the general case the states of the system on either side of the potential barrier are different and this alters the situation radically. Only when the tunnelling species is in a free state on either side of the barrier and is described by a planar wave is its passage through the barrier a non-resonance process and its probability varies monotonically with energy. However, a chemical reaction in no way constitutes a transition of a planar wave through the barrier, but is associated with the transition of a species or a group of species from one potential well to another—above the barrier separating these wells or through it.

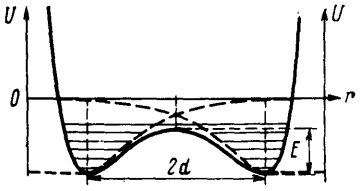

Figure 4. Schematic illustration of the barrier formed by the superposition of two "opposed" Morse potential curves.

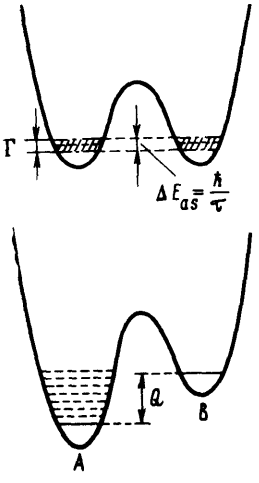

Figure 5. Schematic illustration of the distribution of energy levels in two identical and different potential wells.

The energy states of the system in each potential well are quantised; they are characterised by a set of discrete levels and tunnelling is possible only under resonance conditions, i.e. when the levels are the same in both wells. This can be illustrated by Fig. 5. If two identical "traps" which may contain an electron, for example two protons, are brought closer together, we obtain a system of two equivalent potential wells. In each of these traps taken separately the electron would exist at a certain stationary level (infinitely narrow in the ground state). In the presence of a system of two completely identical wells, the electron is delocalised—it tunnels continuously from one well to the other, and the characteristic time of such subbarrier transition τ_0 is shorter the narrower and lower the barrier separating the wells. Neither the residence of the electron in the left-hand well nor its presence in the right-hand well constitute any longer stationary states of the system and the levels of the electron in each well now have a finite width $\Gamma = \hbar/\tau_0$. In other words, neither the wave function Ψ_l (electron in the left-hand well) nor the function Ψ_r (electron in the right-hand well) are any longer eigenfunctions of the system; such functions are now their combinations—symmetrical: $\Psi_s = (1/\sqrt{2})[\Psi_l + \Psi_r]$, and antisymmetric: $\Psi_a = (1/\sqrt{2})[\Psi_l - \Psi_r]$. This implies that the system can exist in two states differing in energy by $\Delta E_{as} = \hbar/\tau$ (Fig. 5) and the two states Ψ_s and Ψ_a are the same and coincide with Ψ_l and Ψ_r only when $\tau \to \infty$ (when the two wells move apart to an infinite distance).

However, the absolute identity of the two wells is exceptionally rare or altogether impossible†. On the other hand, in the general case when the two wells differ, the levels in them become non-stationary and tunnelling transitions between the wells are possible only when the levels coincide to within $\Delta E = \hbar/\tau$, where $\tau \geqslant \tau_0$; τ_0 is the tunnelling time in the idealised case of identical wells, i.e. for an absolutely symmetrical barrier.

We shall now consider the general case of two different wells for an exothermic transfer of a certain species m between molecules A and B : $A + Bm \to Am + B$. To make the treatment specific, we shall assume that m is an electron, A an oxidant, and Bm a reductant. Since we are interested in the region of low temperatures, we shall further assume that in the initial state all the molecules Bm are in the lowest energy level—the level of zero-point vibrations.

If the level nearest (from below) to the initial level in potential well A is separated from the latter by a distance $\Delta E \gg \Delta E_0$, where $\Delta E_0 = \hbar/\tau_0$, then under adiabatic conditions, i.e. in the absence of interactions between electrons, the nuclei of the molecules A and B, and the surrounding medium, a tunnelling transition is impossible and the state of the electron in well B is stationary (to within a negligibly low rate of the radiation-induced transition: $A + Bm \to Am + B + h\nu$). In fact, under such conditions, there is simply no place to which the energy of the transition ΔE could be transferred.

For the transition to become possible, it is necessary to find a "sink" for this energy or to modify the form of the potential wells (and hence the positions of the levels in them) in such a way that the levels coincide in the two wells, i.e. the condition $\Delta E \leqslant \Delta E_0$ holds. The transfer of the energy ΔE both to an individual molecule and to the crystal lattice can serve as a "sink". In the region of low energies (when $\Delta E \leqslant 0.02$ eV) the dissipation of the energy ΔE is associated with the excitation of the vibrational lattice quanta—phonons. In the present instance we are considering the "softest" region of the vibrational lattice spectrum—its acoustic branches, and there is a

† For example, even the transfer of an electron ($H + H^+ \to H^+ + H$) or an H atom ($H + H_2 \to H_2 + H$) might be regarded as a transition between two absolutely identical wells only in terms of the approximation of a complete absence or a complete equality of the interactions [interaction energies?] of H and H^+ on the one hand and H and H_2 on the other with the surrounding medium, which is not as a rule the case.

possibility not only of single-phonon but also of multiphonon transitions, in particular two-phonon transitions with absorption of the energy ΔE. For large energies (up to 0.2–1 eV), the energy ΔE is consumed in the excitation of normal vibrations in molecules or of high-frequency, optical branches of the vibrational spectra of the molecular crystal lattices.

The interaction of electrons and nuclei, responsible for the dissipation of the electronic excitation energy via vibrational degrees of freedom, permits non-adiabatic electronic transitions in which the Franck–Condon principle does not hold and the internuclear distance changes. At the same time the interaction of electrons and nuclei broadens the levels approximately by the factor $\sqrt{M/m}$, where M is the mass of the nucleus and m the mass of the electron, and this also promotes tunnelling, decreasing ΔE as a result of the possibility of the mutual approach and overlapping of the edges of the broadened levels. The broadening of the levels occurs also due to the interaction of the molecules with their environment (which is characteristic of a condensed phase), when the system comprising two potential wells is no longer adiabatic. Such interaction in fact leads to the appearance of a band in the optical branches of vibrational lattice spectrum instead of the vibrational spectral lines due to individual molecules.

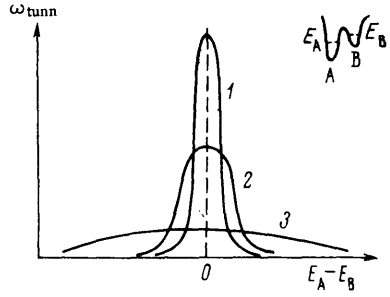

Figure 6. Illustration of the broadening of the levels and of the corresponding decrease of the maximum probability of resonance transitions ω_{tunn}; $(\Gamma A)_1 < (\Gamma A)_2 < (\Gamma A)_3$.

As happens in any type of level broadening, the probability integral for the transition to each given level remains unchanged and consequently the maximum resonance probability of the transition characteristic of narrow levels decreases sharply (Fig. 6). The situation with an extremely high probability of tunnelling transitions within narrow resonances, associated with a complete absence of such transitions between resonances, is replaced by a much weaker (i.e. slow) tunnelling transition over a wide range of energies, which, however, depends little on the excitation energy. The exponential decrease of reaction rate with decreasing temperature should therefore be gradually retarded, reaching a plateau, as in the case of two identical wells; however, even at $T \to 0$ there remains a finite and sometimes measureable probability of a tunnelling transition from the zero-point vibrational level in the initial potential well to the virtually continuous spectrum of vibrations in the final potential well.

Another variant of tunnelling transitions—as a result of the equalisation of the levels in the two wells ($\Delta E \lesssim \Delta E_0$)—is associated with the fluctuations in time of the magnitude of the polarisation interaction of Am and Bm with the surrounding medium, for example the interaction of charged molecules with the dipoles moving around them[6,7]. Such fluctuations correspond to a time dependence of the configurations (depths and shapes) of both potential wells shown in Fig. 5. The levels in the two wells are then displaced (over a period of time) upwards and downwards and in the course of such displacement the positions of the levels in A and B may coincide for a brief period, which implies the occurrence of the resonance condition necessary for tunnelling. However, in this variant the fluctuations are frozen at very low temperatures and, when the levels in the "frozen" wells do not overlap and interaction with the surrounding medium (discussed above) is not included, the rate of reaction tends to zero or more precisely to an extremely low value characteristic of radiation-induced transitions.

Thus, although the quantum-mechanical properties of the substance, namely the presence of the zero-point vibrational level, and the tunnel effect involving transitions through potential barriers lead in principle to the possibility of chemical reactions even at the very lowest temperatures, one can in no way assert *a priori* that chemical reactions can occur at measureable rates in the vicinity of the absolute zero. Only experiments can provide an answer to this question.

III. EXAMPLES OF THE TUNNELLING OF HYDROGEN ATOMS AND ELECTRONS AT LOW AND VERY LOW TEMPERATURES‡

All experimental studies on the problem of tunnelling transitions carried out until recently can be divided into two groups depending on whether processes involving the transfer of hydrogen atoms or electrons were observed.

The available data (quantitative or semiquantitative) for hydrogen-atom transfer reactions, which may indicate an appreciable contribution of tunnelling transitions, are listed in the Table. Among these data, the most complete results were obtained in a study of the displacement of the free-radical state in the radical pairs of γ-irradiated dimethylglyoxime (Yakimchenko and Lebedev[8]). It was shown that the temperature variation of the rate of reaction becomes much less pronounced at low temperatures—the observed activation energy falls from 7.3 kcal mole^{-1} at 190–220 K to 1.4 kcal mole^{-1} at 77–110 K and in addition a marked retardation (by 3–5 orders of magnitude) of the substitution of hydrogen by deuterium is observed. Thus the presence of the tunnel effect was clearly demonstrated. Comparison of the experimental data with the present authors' 1959 calculations[4] (Fig. 7) made it possible to determine the parameters of the activation barrier: $E = 15 \pm 1$ kcal mole^{-1} and $d = 0.6 \pm 0.1$ Å.

‡ The concept of "low temperatures" is fairly arbitrary and in addition is different in physics and chemistry. In physics low temperatures are usually understood as temperatures below 4 K (liquid helium). In chemistry the temperature range from 195 K (dry ice) to 77 K (liquid nitrogen) is referred to as low temperatures, while temperatures below 77 K are regarded as ultralow.

However, all the experimental data on tunnelling by hydrogen atoms so far refer to relatively high temperatures (in excess of 77 K) and the attainment of a plateau by the rate of such reactions has not been observed in any investigation—the observed activation energy has not been less than about 0.05 eV. The attainment of a limiting rate at low temperatures (down to 4.2 K, with a direct determination of the rate) has until very recently been observed only in electron transfer processes. Thus De Vault and Chance[9,10] and Grigorov[11] demonstrated that the rate of electron transfer from cytochrome *c* to chlorophyll is independent of temperature in the range 4.2–77 K (Fig. 8). The present author investigated[12] the trapping of electrons by O^- ions in irradiated alkaline ice and showed that the rate of such trapping $e^-_{tr} + O^- \rightarrow O^{2-}$ does not change between 4.2 and 120 K.

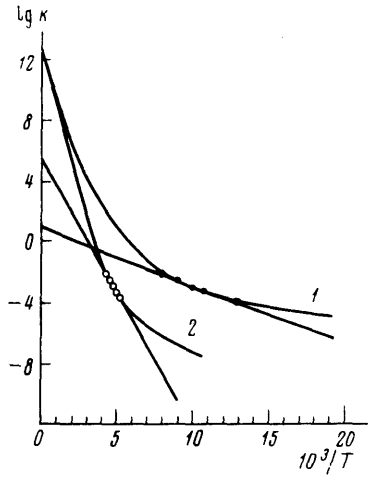

Figure 7. Calculated and experimental temperature variation (in terms of the Arrhenius coordinates) of the rates of reactions involving the transfer of hydrogen atoms (curve *1*) or deuterium atoms (curve *2*) in γ-irradiated dimethylglyoxime crystals.

In all similar cases one is dealing with the tunnelling transfer of electrons over large distances, amounting to several tens of angstroms (for $d \simeq 30$ Å and $E \simeq 1$ eV, we have $T_t \simeq 160$ K). The occurrence of such transfer explains the large radii corresponding to the trapping of electrons by acceptors[13] and the low concentrations of the ionic species stabilised on radiolysis[14] and holds out great promise that a whole series of new kinetic phenomena may be discovered. For example, in the low-temperature radiolysis of solid organic substances a decrease of the probability of electron stabilisation should be observed with increase in the concentration of traps in excess of limiting concentrations of ions, $[T] > [I]_{lim}$, since, under conditions where the distance between traps is less than the distance of effective tunnelling transfer, an electron tunnelling from one trap to another will roll down towards the cation B^+. Another, more "chemical" effect is associated with the fact that the displacement of the reactants in solid-phase reactions usually takes place at very low frequencies ($\nu_m \simeq 1\ s^{-1}$) and therefore species with charges of different signs (A^- and B^+) will neutralise one another in consequence of electron transfer by tunnelling before they meet in the reaction cage, i.e. while there are still several layers of neutral matrix molecules M between them.

$$A^- + M + B^+ \rightarrow A + M + B\ .$$

The subsequent reaction, if it occurs at all, would now involve a homolytic mechanism.

Thus, by ensuring the occurrence of reactions between spatially separated species in the solid phase, the tunnel effect can alter the reaction mechanism and even the final radiolysis products formed. Estimates have demonstrated the possibility of this type of electron trapping and of the separation in time of charge recombination processes and the subsequent chemical reaction even in viscous liquids. In general, in the liquid phase the tunnel effect weakens significantly the influence of the electrostatic interaction between reactants bearing charges of the same sign.

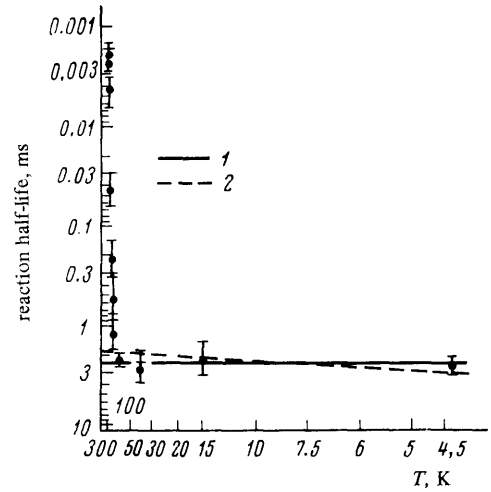

Figure 8. Experimental data of De Vault and Chance[9,10] for the rate of oxidation of cytochrome *c* by chlorophyll at different temperatures: 1) $E = 0$; 2) $E = 4$ cal mole^{-1}.

In polymer chemistry and in biochemistry the tunnel effect can ensure electron transfer between macromolecular fragments which cannot collide, for example because of steric hindrance. A theoretical interpretation of electron transfer by tunnelling over large distances between complex biological molecules with allowance for the possibility of simultaneous conformational changes in these molecules has been recently developed by Chernavskii, Blyumenfel'd, and other Soviet workers (see, for example, Refs. 15 and 16) and we shall return to this topic.

However, it must be emphasised that so far electron transfer from one species to another can hardly be called a genuine chemical reaction. Such a reaction necessarily involves a rearrangement of atoms or at least a change in valence bond lengths and in the corresponding angles, i.e. a displacement of atoms in space.

Reactions with transfer of hydrogen atoms by tunnelling.

Reaction	T, K	Pre-exponential factor Z, s^{-1}	E, cal $mole^{-1}$	System	Remarks
$HON[C(CH_3)_2]NO^{\cdot} \rightarrow ON[C(CH_3)_2]NOH$, i.e. $R:NO^{\cdot} + R:NOH \rightarrow R:NOH + R:NO^{\cdot}$	77—110	H:1.5	1400±70	γ-Irradiated dimethylglyoxime single crystals	O.E.Yakimchenko and Ya.S.Lebedev, Int. J. Rad. Phys. Chem., 3, 17 (1971)
	190—220	D:6·10⁴	7300±700		
	270—310	H:3·10⁴	17700±700		
	310—340	D:1.7·10¹³	24200±400		
$\dot{C}H_3 + CH_3CN \rightarrow CH_4 + \dot{C}H_2CN$	77—87	$(k^H/k^D > 140$ at 87 K)	1400±100	γ-Irradiated acetonitrile	R.J.Le Roy et al., J.Phys. Chem., 76, 546 (1972)
$\dot{C}H_3 + \sim Si(CH_3)_2-O \sim \rightarrow CH_4 + \sim Si(\dot{C}H_2)-O \sim$	77—105	H:$10^{0.6}$	1500	Polyphenylmethylsiloxane (amorphous phase)	E.L.Zhuzhgov, Thesis, Novosibirsk, 1973
		H:$10^{0.9}$	1500		
		H:$10^{1.5}$	2200	Polydimethylsiloxane (amorphous phase)	
		H:$10^{2.1}$	2200	Polyphenylmethylsiloxane (crystalline phase)	
				Polydimethylsiloxane (crystalline phase)	
$\dot{H} + \sim C(CH_3)_2CH_2C(CH_3)_2 \sim \rightarrow H_2 + \sim C(CH_3)_2\dot{C}H \cdot C(CH_3)_2 \sim$	100—150	H:$10^{8.2}$	2000±400	Reaction on the surface of polyisobutylene	A.M.Dubinskaya and P.Yu.Butyagin, Dokl. Akad. Nauk, SSSR, 211, 141 (1973)
$\dot{H} + \sim CH_2CH_2O \sim \rightarrow H_2 + \sim CH_2\dot{C}HO \sim$	100—150	H:$10^{4.9}$	1200±300	Reaction on the surface of polyepoxyethane	

IV. RADIATION-INDUCED SOLID-PHASE POLYMERISATION AT LOW AND VERY LOW TEMPERATURES

Typical examples of chemical reactions in the full sense of this word include polymerisation reactions. These are chain reactions: after the appearance under the influence of light, radiation, or other factors of the primary active centre, i.e. after the endothermic chain initiation step, the subsequent exothermic chain propagation process, ending in chain termination, takes place spontaneously.

It is not surprising that low-temperature solid-phase polymerisation (particularly radiation-induced polymerisation, i.e. initiated by penetrating radiation) has long attracted the attention of investigators. The first example of such polymerisation was the observation of the radiation-induced polymerisation of solid acrylamide by Mesrobian et al. in 1954[17]. Subsequently a number of fundamental studies on solid-phase radiation-induced polymerisation at low temperatures were carried out by Magat, Shapiro, and others in France, by Okamura, Tabata, and others in Japan, and by Bamford and others in England.

The history of the early studies on this problem has been discussed in a number of monographs and reviews (see, for example, Refs. 18–25) and there is therefore no point in considering it in detail here. A common feature of these early investigations was that the yield of the polymer from a particular radiation dose on the frozen monomer at a specific low temperature was not determined at the experimental temperature but only after heating and fusion of the irradiated monomer. As a result, it remained uncertain, even in those cases where the slope of the curves relating the yield of the polymer to the irradiation dose [characterising the radiation yield of the polymerisation (i.e. the number of polymerising molecules G per 100 eV of the radiation energy)] was independent of temperature, whether this was not caused, for example, simply by the fact that during the low-temperature irradiation only the initial active polymerisation centres are generated, while the polymeric chains grow after irradiation or even during the warming process, for example, always at the same temperature (at the melting point).

The next stage was the investigation of the solid-phase polymerisation of a number of monomers at the Institute of Chemical Physics of the USSR Academy of Sciences, where the usual gravimetric determination of the yield of polymers after warming the irradiated monomers was supplemented by monitoring the warming process calorimetrically[25–28]. Since it was impossible to observe under these conditions the additional heat evolution due to polymerisation, it was concluded that the solid monomers were polymerised directly in the course of irradiation. The results of such experiments are presented in Fig. 9. Seemingly they lead to the conclusion that there is no activation energy for the polymerisation of many solid monomers even at relatively high temperatures—from the melting point down to liquid nitrogen temperature. Subsequently it was, however, shown that at that time such a conclusion would have been premature and unjustified.

In many cases the temperature variation of the yield of the radiation-induced solid-phase polymerisation was found to differ significantly from a simple plateau and depended markedly on the phase state of the irradiated monomers (the example of acrylonitrile proved to be particularly complex[29,30]). It became clear that the sensitivity of the calorimeters used in the investigations[25–28] was far too low to ensure the observation of postpolymerisation during the warming process.

Finally, it must be specially emphasised that the temperature independence of the polymerisation radiation yield (it was in fact this quantity and not the true rate of propagation of polymer chains that was determined in all the investigations where the polymer yield–radiation dose curves were measured) does not by itself demonstrate that the low-temperatures solid-phase polymerisation is a non-activated process, because the radiation yield G depends (this will be discussed further below) on two kinetic constants—the rate constants for the propagation and termination of polymer chains—and the temperature variation of G is accordingly determined by at least two fundamental activation energies. Even the most accurate measurements of the slopes of the polymer yield–dose curves (i.e. the determination of the radiation yields of polymerisation) cannot alone provide information about the rate of polymerisation, but they do give information about the rate constants for the fundamental polymer chain propagation and termination processes and about the presence or absence of activation energy in these fundamental processes as long as the time resolution of the measuring method does not become shorter than the characteristic time of the polymer chain propagation process. It became clear that it is necessary not only to improve sharply the accuracy of the calorimetric method

but also to decrease at the same time its inertia, so that one must learn to observe the magnitude and rate of heat evolution during irradiation itself rather than during the postpolymerisation and heating of the irradiated monomers. Since the retardation of any activated processes must be manifested more clearly the lower the temperature of the medium, the extension of research on radiation-induced solid-phase polymerisation to lower temperatures—to liquid helium temperature (4.2 K)—became extremely urgent.

In 1965 Abkin and coworkers at the Karpov Physicochemical Institute observed the formation of polymers in tetrafluoroethylene and acrylonitrile irradiated at liquid helium temperature[31]. Almost simultaneously a group of investigators at the Institute of Chemical Physics submitted for publication reports of the formation of polymers in acrylonitrile and hexamethylcyclotrisiloxane irradiated at 4 K.[32] Both publications appeared at the beginning of 1966. However, in the light of what has been said about the apparent absence of an activation energy in radiation-induced solid-phase polymerisation above 77 K (Fig. 9), it is clear that these data[31,32] could not provide an answer to the question whether the polymers were really formed during irradiation at liquid helium temperature (they were even less likely to yield the rate of propagation of the polymer chain under these conditions) or in the subsequent process during heating. Thus the problem of the possible direct polymerisation in the vicinity of 4 K continued to remain controversial.

A number of interesting studies designed to solve this problem were carried out in subsequent years by Abkin and coworkers. They investigated the polymerisation of four monomers: tetrafluoroethylene (TFE), acrolein, vinyl acetate, and acrylonitrile; the study of the first two substances was particularly detailed. Experiments involving the addition of inhibitors to TFE irradiated at low temperatures or its "bleaching" (irradiation with visible or ultraviolet light leading to the destruction of active polymerisation centres) made it possible to separate the polymerisation effects during irradiation and postpolymerisation. After the application of corrections for postpolymerisation, the polymerisation yield at 77 K was found to be close to 2% (for an irradiation dose of about 50 Mrad).[33] As regards irradiation in liquid helium, "additional data indicating the formation of small amounts of polymer in the TFE crystal irradiated at 4.2 K were obtained with the aid of the radiothermoluminescence method".[33] This conclusion was supported also by the formation of fluoroalkyl macroradicals of the type $\sim CF_2-\dot{C}F-CF_2\sim$ detected by ESR in the irradiation of TFE near 4 K.[34]

Acrolein was a second object of detailed study by Abkin and coworkers[35,36]. Using the variation of the relative contributions of the isotactic and syndiotactic addition of new units to the growing polymer chain with the irradiation temperature of the solid monomer, which they observed by infrared spectroscopy, the authors[35-38] showed that part of the polymer is formed directly during irradiation even at the temperature of liquid helium. The initial macroscopic rate of polymerisation, defined as $dP/dt = (k_i k_p/k_t) I[M_0]$ {where k_i, k_p, and k_t are the rate constants for polymer chain initiation, propagation, and termination respectively, I is the intensity of ionising radiation (dose rate), and $[M_0]$ is the initial monomer concentration} was about 0.1% h^{-1} at I = 1800 rad s^{-1}.[37]

In their interpretation of the results of these experiments, the authors[37] concluded that the formation of polyacrolein at very low temperatures indicates an appreciable

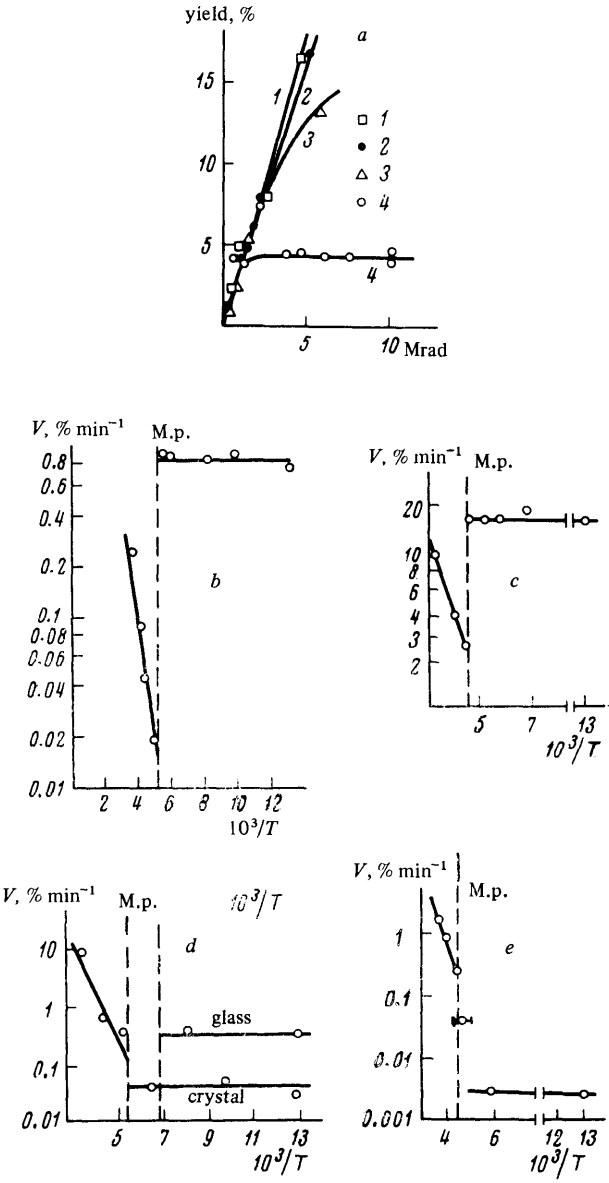

Figure 9. *a*) Variation of the polymer yield with radiation dose for acrylonitrile (AN) in the solid state at different temperatures [temperature (K): 1) 166; 2) 153; 3) 133; 4) 77]; *b*)–*e*) variation of the initial slope (V) of the polymer yield–radiation dose curves with the reciprocal of temperature for four monomers according to data obtained in studies[26-28] in which the gravimetric determination of the yield of polymer in warmed irradiated monomers was supplemented by the calorimetric monitoring of the warming process [*b*) AN, $I \simeq 0.3$ Mrad min^{-1}; *c*) formaldehyde (FA), $I \simeq 10$ Mrad min^{-1}; *d*) vinyl acetate (VA), $I \simeq 10$ Mrad min^{-1}; *e*) methyl methacrylate (MMA), $I \simeq 0.75$ Mrad min^{-1}]. The plateau at low temperatures (apparent absence of activation energy) corresponds to the following radiation yields of the polymerisation reaction: $G \simeq 400$ (AN), $G \simeq 10$ (VA—glass) and $G \simeq 1$ (VA—crystal), $G \simeq 5 \times 10^8$ (FA), and $G \simeq 3$ (MMA). The data in this figure were taken from studies carried out at the Institute of Chemical Physics of the USSR Academy of Sciences at the beginning of the 1960's.[25-28]

mobility of the monomer molecules in the irradiated crystal, and the attainment of a "limiting" yield of the polymer (i.e. the appearance of a plateau on the yield–dose curves) at very low percentage conversions suggests that only a small fraction of monomer molecules exhibit this type of high mobility. Abkin and his coworkers expressed the view that mobile molecules of this kind are distributed in the regions of dislocations and extended defects at the monomer grain boundaries and that in such regions diffusion is considerably facilitated and may proceed virtually without activation energy.

Analysing the role of ionising radiation in low-temperature polymerisation processes, Abkin and coworkers concluded that, "in solid-phase polymerisation the effect of radiation is manifested not only in initiation steps but also in chain propagation reactions as a result of the transformation of the radiation energy into the kinetic energy of the molecules localised near dislocations"[30]. They believe that, together with radiation, the energy of polymerisation itself is a factor which may ensure chain propagation: "radiation-induced polymerisation in the crystal is possible only as a result of the conversion of the radiation energy into the energy of intermolecular motion. This conversion is probably only the initial step in the growth of the polymer chain; subsequently chain propagation takes place owing to the energy evolved on polymerisation".[40]

Calculation (from the numerical characteristics of the relations between the yield and dose indicated above) of the so called radiation yields of polymerisation G, i.e. the number of molecules polymerising per 100 eV of the radiation energy, gives the following values: $G \simeq 4$ for TFE at 77 K and $G \simeq 2.5$ for acrolein at 4 K. Much higher radiation yields are usually characteristic of chain reactions. However, on the hypothesis that polymer chains cannot grow throughout the crystal but only at dislocations and extended defects, the yield of the polymer must be attributed only to the part of the energy absorbed in regions capable of polymerisation and not to the entire radiation energy absorbed by the solid monomer, which may significantly increase the values of G compared with those quoted above.

The development of the present author's research, in which the observation of the formation of a polymer in monomers irradiated at liquid helium temperature was continued[32], followed different paths. The author assumed the necessity for a direct determination of the rate constants for the propagation (k_p) and termination (k_t) of polymer chains.

The length of kinetic chains ν is determined by the ratio of the probabilities of the propagation and termination of these chains: $\nu = k_p/k_t$. The macroscopic rate constant for the accumulation of the polymer in the irradiated monomer, determined from the yield–dose curves, is a complex quantity, which, as stated above, is defined by the expression $k = k_i k_p/k_t = k_i \nu$. Therefore the absence of a temperature variation of this effective constant (or in other words the independence of the radiation yield of the polymer G of temperature) by itself implies merely a small difference between the activation energies for chain propagation and termination, but not that each of these quantities is itself small.

Another variant of solid-state polymerisation involving an apparent absence of activation energy is possible. It was pointed out by the present author as early as 1963–1965[26–28] to explain the apparent absence of activation energy in the solid-phase polymerisation of a number of monomers illustrated in Fig. 9—from the melting point down to 77 K: "We are dealing with a polymerisation mechanism in which the chain length is not determined by the competition between chain termination and propagation at each unit but by some kind of steric conditions, i.e. when the chain length is predetermined by the properties of the material. All temperature dependence then disappears from the expression for the rate of radiation-induced polymerisation $\{k_i I[M_0]\nu\}$, where the only temperature-dependent term is usually the chain length. However, in this case the chain propagation time is determined by the presence of activation energy in each unit of the chain ..."[26,28].

In the light of these considerations, the present author's aim was to determine directly the propagation time of the polymer chain $\tau = 1/k_t = \nu/k_p$ and its temperature variation in order to establish how temperature influences the duration of the fundamental polymer chain propagation steps $\tau_0 = \tau/\nu = 1/k_p$, whether or not the rates of these fundamental steps tend to a limit or become vanishingly small as the temperature is reduced.

V. LOW-TEMPERATURE RADIATION-INDUCED POLYMERISATION OF FORMALDEHYDE. THE OBSERVATION OF THE LOW-TEMPERATURE LIMIT TO THE RATE OF CHAIN PROPAGATION

In a series of studies in 1971–1972 by a group of workers at the Institute of Chemical Physics and the Branch of the Institute at Chernogolovka, including Barkolov, Kaplan, Kiryukhin, and the author of the review, it was possible to observe for the first time the phenomenon of the low-temperature limit to the rate of the chemical reaction in the radiation-initiated polymerisation of formaldehyde (FA). Here the fundamental chemical polymer chain propagation step may be, as shown in Fig. 10, the tunnelling transfer of either an electron or a hydrogen atom. However, in both cases the polymerisation should be accompanied by the approach of the formaldehyde molecule as a whole to the polymer chain, since the density of polyformaldehyde is higher than that of the initial monomer. Consequently the fundamental polymer chain propagation step involves a decrease in the effective distance between neighbouring CH_2O groups by an amount $\Delta\bar{a} = \bar{a}_0 - \bar{a}_f$, where $\bar{a}_0$ is the corresponding distance in the monomer crystal and $\bar{a}_f$ in the polymer chain. At the same time the valence angles of the CH and CO bonds are also altered. Thus in this case the fundamental chemical reaction step takes place in the full sense of the word.

In a series of the present author's experiments on the low-temperature radiation-induced polymerisation of formaldehyde in the solid phase[41–44] by a calorimetric method, the polymer chain propagation time was determined directly. At temperatures exceeding 80 K this time was found with the aid of an adiabatic low-inertia film calorimeter[42]. The design of the calorimeter is illustrated in Fig. 11. It consisted of an aluminium disc *1* 20 mm in diameter and 0.05 mm thick. A resistance thermometer *2* and a calibration heater *3* were glued to the lower side of the disc. The disc was suspended on thin conducting leads within a copper heat shield *4*. The entire assembly was placed in a glass vacuum jacket provided with a carbon adsorption pump *5*. The complete calorimeter was placed in a Dewar vessel containing liquid nitrogen.

Gaseous formaldehyde was frozen onto the calorimeter disc via a heated Kovar capillary *6*. The weight of the test substance in the experiments using this calorimeter

was varied from 15 to 75 mg, which corresponded to a layer thickness on the calorimeter disc of 0.1–0.5 mm. In order to record the calorimeter signal, a multichannel moving coil oscillograph was used. In the determination of the inertia of the calorimeter the calibration current pulse and the calorimeter response were recorded simultaneously on the same apparatus. The calibration was achieved in two ways—with the aid of the calibration heater and by heating the calorimeter by γ-radiation (this leads to uniform heating of the calorimeter disc with the monomer). Fig. 12 shows that the inertia of the calorimeter was 0.3–0.5 s.

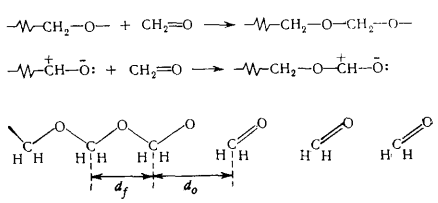

Figure 10. Fundamental processes and a simplified schematic geometrical illustration of the polymerisation of formaldehyde.

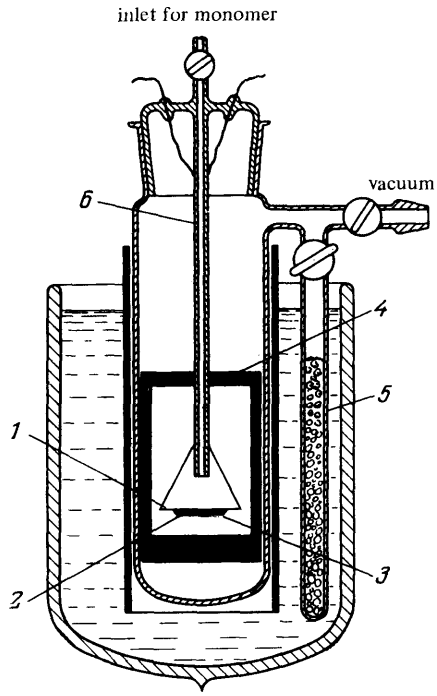

Figure 11. Schematic illustration of the low-inertia adiabatic film calorimeter.

Most of the present author's experiments on radiation-induced polymerisation were carried out using the γ-radiation from ^{60}Co apparatus. However, since the radiation sources in this apparatus were raised mechanically to the working position so that the dose rate reached a maximum in 60–70 s, the kinetics of the initial polymerisation stage might have been distorted by the change in the intensity of the initiating radiation with time. To avoid this, the bremsstrahlung from an electron accelerator with an energy of 5 MeV was used to initiate the polymerisation in the above experiments. This radiation source could be switched on and off in only a few microseconds.

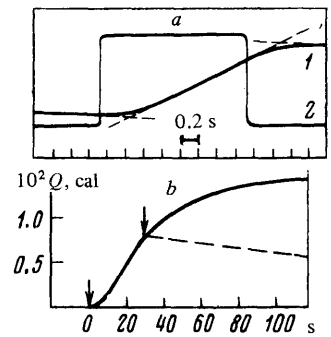

Figure 12. *a*) Calibration oscillogram for the film calorimeter [1) time variation of the calorimeter signal; 2) current flowing through the calibration heater of the calorimeter]; *b*) kinetics of heat evolution in the polymerisation of formaldehyde in the field of γ-bremsstrahlung [temperature 80 K; weight of formaldehyde 0.03 g (thickness of layer approximately 0.2 mm); dose rate 7 rad s^{-1}]. The arrows indicate the instants when the electron beam was switched on and off. Dashed line—calorimeter signal in the calibration experiment.

Initially the dose rates of the bremsstrahlung were measured with the aid of a film calorimeter—they varied linearly in the range from 3 to 40 rad s^{-1} with increase of the electron current on the stopping target from 1 to 12 μA. Fig. 12 presents the results of experiments on the polymerisation of solid formaldehyde in the bremsstrahlung field. The rate of polymerisation reached a constant value (the attainment of a linear increase of heat evolution with time) in 2–3 s; this is also the polymer chain propagation time, after which the rate of chain termination is equal to the rate of the radiation-induced initiation, i.e. the number of chains growing simultaneously in the system becomes constant.

In the temperature range 4–80 K a diathermal calorimeter, the design of which is illustrated in Fig. 13, was used to measure the polymer chain propagation time in solid formaldehyde. The calorimeter shell consisted of a thin-walled Kovar capillary *1* (2 mm in diameter), which was evacuated after the introduction of the monomer, filled with the helium heat exchanger, and sealed off. A calibration heater *2* was wound on the outer surface of the Kovar capillary and a copper–gold–iron thermocouple *3* was attached. The thermocouple recorded to within 0.5 K the temperature drop across the diathermal shell, i.e. between the calorimeter shell *1* and the copper shield *6*, which was in thermal contact with liquid helium, i.e. was at a temperature of 4.2 K. Thus the absolute measurement of experimental temperature was achieved with the aid of this capillary at the All-Union Institute of

Physicotechnical and Radiotechnical Measurements (VNIIFTRI) in accordance with a USSR State Standard. The calorimeter was suspended in a glass vacuum jacket *4* surrounded by the copper shield. The entire assembly was placed in a helium bath within a glass cryostat *5*, so that the temperature could be varied by raising the capillary with the formaldehyde to a particular height above the level of liquid helium in the bath and also by balancing the evaporator heater and the calorimeter heater. The calorimeter was calibrated both with the aid of the calibration heater and by heating the calorimeter by the γ-radiation itself, a special low-inertia device with a dropping lead diaphragm for rapid (about 0.05 s) application of the radiation field being used in these experiments.

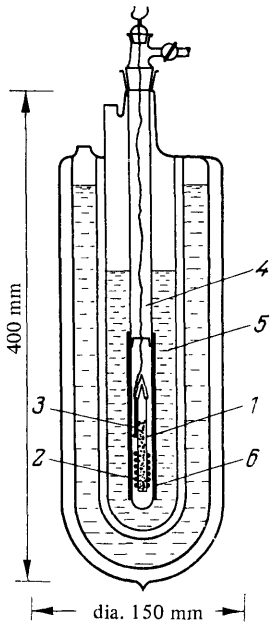

Figure 13. Schematic illustration of the diathermal calorimeter used in low-temperature experiments.

By fitting the $W = W_0(1 - e^{-t/\tau})$ curve to the plot in Fig. 14 (curve *1*) of the increasing rate of polymerisation after switching on the initiating radiation, it was possible to determine the characteristic process time τ, i.e. the average polymer chain propagation time in formaldehyde. Below 10 K, this time approached 10 s. Analogous experiments with polyformaldehyde, which was heated entirely by the absorption of γ-radiation, made it possible to measure the characteristic calorimeter time τ_c at different temperatures ($\tau_c \simeq 1$–4 s at 4–20 K)—see curve *2* in Fig. 14.

For a correct interpretation of the experiments carried out near the helium temperature (5–20 K), the problem of the possible increase of temperature within the irradiated monomer block as a result of the radiation energy and heat of polymerisation is extremely significant. The heat capacity of a substance near the absolute zero decreases sharply as the temperature is reduced. An idea about the maximum possible temperature rise within the monomer block can be obtained by estimating the adiabatic temperature rise in the system during 2–3 s, i.e. the period during which thermal equilibrium was established in the system. There are no literature data for the heat capacities of solid formaldehyde. Using the same calorimeter, the present author estimated the specific heat of formaldehyde at 6–7 K, approximately 2×10^{-3} cal g^{-1} K^{-1} being obtained (the accuracy of these determinations did not exceed 50%). We may note that the result was of the same order of magnitude as the low-temperature specific heats of other organic substances, for example acrylonitrile (6×10^{-3} cal g^{-1} K^{-1} at 10 K) and benzene (0.8×10^{-3} cal g^{-1} K^{-1} at 6 K). It also proved to be close to the estimates based on the Debye approximation, if one assumes that the Debye temperature $\theta \simeq 100$ K, the value determined for a number of molecular crystals.

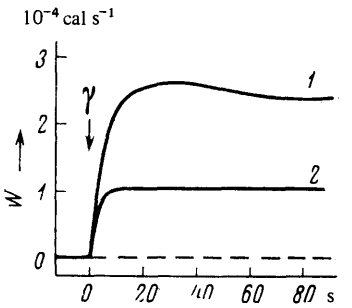

Figure 14. Variation of the rate of heat evolution in the initial period of the irradiation of specimens in the diathermal calorimeter: 1) irradiated tubes with the monomer (0.25 g); 2) irradiated tubes with polyformaldehyde (polymer sample 0.25 g, about 1 g together with tube); dose rate $I = 45$ rad s^{-1}.

Curve *2* in Fig. 14 shows that the heat evolution due to the absorbed radiation (45 rad s^{-1}) in the 0.25 g specimen (about 1 g together with the support) did not exceed 10^{-4} cal s^{-1}. In view of the specific heat of formaldehyde stated above, this corresponds to an adiabatic heating rate of about 0.1 K in 2–3 s. The heat evolution due to the polymerisation of formaldehyde at the above dose rate amounted to about 1.5×10^{-4} cal s^{-1} in a 0.25 g specimen (Fig. 14, curve *1*). This heat evolution was capable of giving rise to a heating rate somewhat higher than that due to irradiation but not exceeding 0.5 K in 2–3 s.

In separate experiments with an adiabatic calorimeter at 80–140 K, the present author determined the heat of polymerisation of formaldehyde, which proved to be 8.5 ± 1 kcal $mole^{-1}$. Having adopted the same value also at lower temperatures and having determined experimentally the rate of heat evolution due to polymerisation at different specified dose rates, the author was able to determine directly the radiation yield G of the low-temperature solid-phase polymerisation. This yield is of the order of 10^7 at 140 K, 10^5 at 80 K, and 10^3 at 4 K. Such high radiation yields, which had never been observed previously at low temperatures, are themselves of considerable interest, demonstrating the possibility of the spontaneous propagation of long chains even in the vicinity of the absolute zero.

However, the values of G combined with experimental chain propagation times are of even greater interest.

In fact, having determined experimentally on low-inertia calorimeters the polymer chain propagation time τ at different temperatures (the variation of $\lg\tau$ with $1/T$ is represented by curve *1* in Fig. 15), the author was able to reach fairly definite conclusions about the average time τ_0 required for the fundamental step involving the addition of a single new link to the growing polymer chain. If the radiation yield of chain initiation, i.e. the yield of the reaction involving the creation of the initial active centres, is g, then in the absence of chain transfer the length of the polymeric molecule is $\nu = G/g$ monomer units and the average time required for the addition of a new link to the chain is $\tau_0 \simeq \tau/\nu$. The efficiency of chain initiation by ionising radiation may be regarded as independent of temperature: $g \simeq$ const. Having put $g \simeq 1$ (the value characteristic of the formation ions or radicals) to make the treatment concrete, we adopted $\tau_0 \simeq \tau/G$ as a fairly accurate estimate. Curve *2* in Fig. 15 represents the variation[45] of $\lg\tau_0$ with $1/T$.

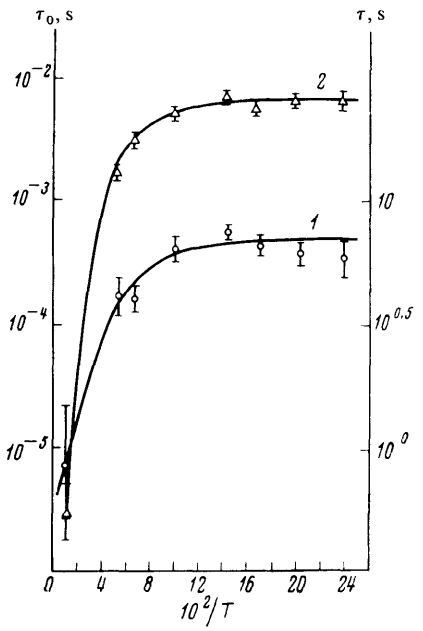

Figure 15. Temperature variation (in terms of the Arrhenius coordinates) of the total polymer chain propagation time τ (curve *1*) and of the average time required for the increment by one new unit of the polyformaldehyde chain $\tau_0 = \tau/G$ (curve *2*).

In the range 80–150 K, τ_0 increases with decrease of temperature in accordance with the Arrhenius law with an activation energy $E \simeq$ 2000–2500 cal mole^{-1} and reaches $\tau_0 \simeq 10^{-5}$ s at 80 K. At lower temperatures there is a marked deviation from the Arrhenius law—the average time required for the addition of a single chain unit tends to the constant value $\tau_0 \simeq 10^{-2}$ s, while extrapolation in accordance with the Arrhenius equation would yield unreasonably large values (about 10^{30} years at 10 K and 10^{100} years at 4.2 K).

The question naturally arises whether or not macroscopic heating of the formaldehyde specimens occurred in the present author's experiments owing to the ^{60}Co radiation energy and the heat of polymerisation. However, the above estimates make it possible to give a quite definite negative answer to this question. In principle, one can imagine the possibility of more marked local heating in regions adjoining the new polymer chain unit just formed, owing to the heat of the fundamental chain propagation step. However, during a period of the order of 10^{-2} s, such heating under the conditions of isotropic heat conduction would have to include a region with a linear dimension of the order of tens of micrometers and is therefore quite negligible.

VI. INTERPRETATION OF THE LOW-TEMPERATURE LIMIT TO THE RATES OF CHEMICAL REACTIONS

Thus a kind of limit has been observed experimentally for the rate of chain propagation in radiation-initiated solid-phase polymerisation of formaldehyde at low temperatures. After this the general problem of the interpretation of the low-temperature limit of the rates of chemical reactions became crucial, because it can be treated in different specific ways.

According to the ideas of Abkin and his coworkers[35-40] quoted above, the growth of polymer chains at low temperatures is not a spontaneous process but is due to the influence of external radiations, which, as it were, "prod" the growing chains. The necessity for such "prodding" leads to a decrease of the radiation yield of the chain reactions from $G = g\nu$ to g. The ambient temperature should then naturally play a markedly secondary role in determining the rate of polymer formation. In the case of the formaldehyde polymerisation reaction investigated by the author, the enormous radiation yields of polymerisation mentioned above constitute evidence against this explanation. However, the decisive objection to the idea that the low-temperature growth of formaldehyde polymer chains occurs as a result of the additional energy supplied by radiation is provided by an experiment carried out very recently at the Institute of Chemical Physics[46] in which postpolymerisation of formaldehyde was observed directly at liquid helium temperature at which the monomer was also irradiated. The diathermal calorimetric technique described above (Figs. 13 and 14) was used in this experiment, but with the difference that, owing to the special magnetic seal employed, it was possible not only to switch on but also to switch off the ^{60}Co radiation field very rapidly, in several hundredths of a second. The positions of the plateaux in the initial parts of curves *1* and *2* in Fig. 16 (curve *1*—for a 0.25 g formaldehyde sample; curve *2*—for the analogous polyformaldehyde sample; the total weight of the irradiated calorimeter cell was about 1.5 g and the dose rate $I \simeq$ 60 rad s^{-1}) show that, in the radiation field at $T \simeq$ 4–5 K, the calorimeter records the polymerisation of formaldehyde with a radiation yield $G \simeq 2 \times 10^3$. After the rapid switching off of γ-irradiation, polymerisation does not cease instantaneously (like heat evolution due to the irradiation of polyformaldehyde, where the characteristic time for the decay of heat evolution is determined by the relaxation of the calorimeter and amounts to approximately 2–3 s for curve *2*), but its rate decreases with a characteristic time (curve *1*) $\tau \simeq$ 10–20 s, i.e. virtually the same as the time needed for the growth in the rate of

polymerisation at liquid helium temperature in the radiation field. Thus the propagation of formaldehyde polymer chains at 4–5 K was demonstrated experimentally also in the absence of irradiation and its rate was determined and found to be virtually the same as in the radiation zone.

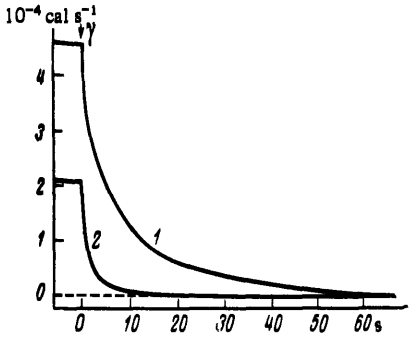

Figure 16. Variation of the rate of heat evolution during the irradiation of specimens in the diathermal calorimeter and after the cessation of irradiation (this instant is indicated by an arrow). Overall weight of the cells with the substance about 1.5 g; weight of formaldehyde (curve *1*) and polyformaldehyde (curve *2*) specimens about 0.25 g; ^{60}Co irradiation dose rate $I \simeq 60$ rad s^{-1}; experimental temperature $T \simeq 4$–5 K.

Semenov suggested that non-activated solid-phase polymerisation processes may develop via the energy chain mechanism involving the migration of an exciton (an excitation quantum) along the growing chain[25,47]. However, under these conditions the linear rate of chain propagation would be expected to be of the same order of magnitude as the velocity of sound in the solid (about 10^5 cm s^{-1}), the time required to add a new link to the growing polymer chain would be $\tau_0 \simeq 10^{-13}$ s, and the total chain propagation time for the above values of G would be in the range $\tau \simeq 10^{-10}$–10^{-6} s. The experimental values of τ are higher by many orders of magnitude.

According to the results of Benderskii et al.,[48] optical phonons traversing relatively large distances arise in molecular crystals under illumination; the time of their conversion into acoustic phonons, i.e. into heat, is fairly long (about 10^{-6} s). Since the end of the growing polymer chain may be regarded as a trap for optical phonons, there is a possibility of an additional supply of energy to the polymer chain from another chain growing at the same time. In this case $\tau_0 \simeq 10^{-2}$ s would no longer represent the time required for the spontaneous increase of chain length by a single unit, but would represent the time required for the addition at the end of the chain of a phonon from some other, "foreign" chain. However, τ_0 would then be inversely proportional to the total number of chains growing simultaneously in the system or, in other words, to the dose rate of the radiation (I) initiating the polymerisation. However, the present authors experiments demonstrated the independence of τ_0 of I.

Ovchinnikov's calculations[48,50] indicate the possibility of the existence in molecular crystals of localised long-lived vibrational states with lifetimes up to several seconds (the results of the calculation for nitrogen N_2 at $T = 30$ K). The slowness of the "de-excitation" of such state is in fact due to the factor already discussed above, namely the non-resonance mechanism of the single-quantum energy transfer from the excited to the non-excited oscillator: owing to the anharmonicity of the intramolecular vibrations, the energy difference between two high levels $\Delta E_n = E_n - E_{n-1}$ is smaller than $\Delta E_1 = E_1 - E_0$ and the transfer of the energy E_n to a non-excited neighbouring molecule is possible only with simultaneous absorption of phonons, i.e. when the lattice energy is employed. In the complete absence of coupling between the two oscillators, the rate of this process would become vanishingly low near the absolute zero, and the lifetime of the molecule at the E_n level would be determined by very slow radiation-induced transitions $E_n \rightarrow E_0$ or by the multiquantum resonance transfer of the entire energy E_n.

The involvement of long-lived vibrational states in low-temperature polymerisation as active terminal groups would require a constant additional energy supply to the growing chain due to its intrinsic heat of polymerisation and its probability would be almost unity [more precisely $(\nu - 1)/\nu$ or $(G-1)/G$]. Furthermore, the available experimental data support the view that the active centres for the growing polymer chain of solid formaldehyde at low temperatures are stabilised long-lived ions rather than any excited states.

When irradiated formaldehyde is warmed outside the radiation zone, the calorimeter detects a fairly rapid postpolymerisation—at lower temperatures the lower the irradiation temperature, the higher the dose, and the more sensitive the calorimeter (as mentioned above, after irradiation at 4 K the present author was able to observe recently postpolymerisation even at the irradiation temperature[46]). However, on optical bleaching of the irradiated specimen, its solid-phase postpolymerisation (before fusion) is completely suppressed. The bleaching effect is in fact characteristic of ions and can be accounted for by their ejection from traps and neutralisation. Hence one may conclude that the active centres in low-temperature formaldehyde polymerisation are ionic.

A characteristic feature of ionic active centres is known to be their involvement in ion–molecule reactions which do not require activation energy and frequently proceed with geometrical or larger cross-sections. The study of such gas-phase reactions was begun by Tal'roze[51,52] and their possible role in the condensed phase has been frequently mentioned in the literature. However, the time required for the addition of a new link to the growing chain of solid polyformaldehyde at low temperatures ($\tau_0 \simeq 10^{-2}$ s at $T \rightarrow 0$), which is too short for a transition over the barrier, is at the same time found to be too long for a barrier-free non-activated transition and makes it necessary to return to the idea of quantum-mechanical transitions through activation barriers with which this review was begun.

Having compared all the experimental data, we shall now consider the explanation of the quantum-mechanical low-temperature limit to the rate of polymerisation of formaldehyde on the basis of tunnelling transitions from the zero-point vibrational level, which are naturally impossible for any endothermic reaction[45]. An attempt will be made below to describe quantitatively this explanation without going into its mathematical details and almost without formulae.

As stated above, polymerisation may involve electron or hydrogen atom transfer, but it is in any case associated with a displacement of the monomer molecule as a whole. The tunnelling displacement of the formaldehyde

molecule over a distance $\Delta d = d_0 - d_f$, is undoubtedly a slower process than the tunnelling by an electron, since $M/m = 5.5 \times 10^4$ (M is the mass of formaldehyde and m that of the electron). As regards the tunnelling by a proton over a distance close to d_0, one cannot claim *a priori* that this process is faster than the tunnelling by formaldehyde over a distance $\Delta d \ll d_0$. However, the present author's direct experiments demonstrated the absence of a significant difference between the rates of polymerisation of normal and deuteriated formaldehyde at low temperatures (about 4 K).[53] On this basis, one may assume that, regardless of the polymerisation mechanism, tunnelling by the formaldehyde molecule as a whole in fact constitutes the rate limiting step for the process at low temperatures.

We shall consider the addition of formaldehyde molecules to a growing polymer chain on the basis of the quantum-mechanical theory of relaxation processes[54-56]. This theory arose mainly in connection with the problem of the radiationless relaxation of excited electronic states in molecules. It is based on the adiabatic Born–Oppenheimer theory and is applicable over an extremely wide range of conditions.

The different states of formaldehyde molecules are represented in terms of the adiabatic approximation by the potential curves in Fig. 17. The adiabatic potential curve a describes the state of the formaldehyde molecule joined to the growing polymer chain, curve b_1 represents the state of the initial monomer molecule, and curve b_2 represents the state of the next, neighbouring molecule (the zero on the abscissa axis is displaced to the right for this curve by an amount $\Delta d = d_0 - d_f$). Curves a and b_1 and b_1 and b_2 do not intersect. According to the rules of quantum mechanics, such intersection is prevented owing to the occurrence of particular interactions in the system described by the curves and instead of their intersection a gap arises between them.

At the initial instant the two monomer molecules are in states b_1 and b_2 and well a is vacant. Within the framework of the adiabatic approximation, this situation corresponds to a stable stationary state§, since none of the levels in well b_1 (at ultralow temperatures only the zero-point vibrational level is populated in this well) overlaps with any of the levels in the deeper well a.

In other words, not only are the monomer molecule and the growing polymeric active centre themselves stable in isolation, but also, in the absence of both a "free" transition over the barrier (i.e. at fairly low temperatures) between the two wells and under the conditions of the overlapping of their levels, even the monomer molecule adjoining the terminal group would be fully stable. However, owing to the interaction of the reacting molecules with the surrounding medium, i.e. owing to energy exchange with the lattice, the situation changes and there arises the possibility of an exothermic chemical reaction, in our example the polymerisation of formaldehyde, even at the absolute zero.

States a and b_1 can be regarded as two different electronic states of the polyformaldehyde active centre (poly-FA*)–formaldehyde system. State a, in which formaldehyde is displaced to the growing chain and there is a rightward "jump" of the terminal free valance, corresponds to the ground electronic state of the system in Fig. 18. State b_1, in which the formaldehyde molecule is separated from the growing polymer chain, corresponds to the electronically excited state. Owing to the interaction of the electrons and nuclei in the poly-FA*–formaldehyde system, the adiabatic approximation breaks down and the $b_1 \rightarrow a$ transition becomes possible, i.e. the system may relax via the chemical chain propagation step. Mathematically such relaxation is related to the presence in the Hamiltonian of a higher-order term involving the small Born–Oppenheimer parameter $\kappa = (m/M)^{1/4}$, called the non-adiabatic operator.

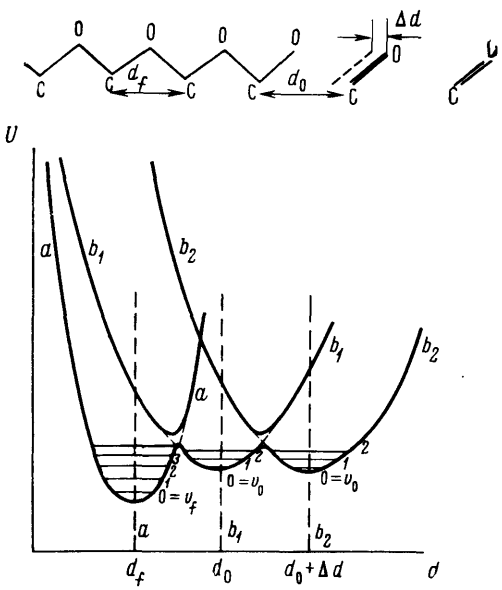

Figure 17. Upper part—simplified schematic illustration of the disposition of the solid FA monomer molecules and of the polymer chain. Lower part—schematic illustration of the tunnelling transitions of the CH_2O groups in polymerisation ($b_1 \rightarrow a$) and in filling the "cavities" arising during polymerisation in the vicinity of the terminal group of the polymer chain ($b_2 \rightarrow b_1$): a) diabatic potential curve for the formaldehyde molecule attached to the growing polymer chain; b_1) analogous curve for the initial monomer molecule; b_2) analogous curve for the next monomer molecule (the zero on the abscissa axis for this curve has been displaced to the right by an amount Δd).

The next formaldehyde molecule can undergo resonance migration from state b_2 to the vacated well b_1 with subsequent addition to the polymer chain ($b_1 \rightarrow a$), etc.

In the initial state (subscript 0) the system is at the level of zero-point vibrations: $\upsilon_0 = 0$, and the vibrational frequency of the monomeric formaldehyde molecule is ω_0, which is much less than the vibrational frequency of the monomeric CH_2–O unit in the final state (subscript f), i.e. in the polymer chain, which is ω_f. Owing to the interaction between the electronic states 0 and f, due to the non-adiabatic operator $\hat{L}$, there is a possibility of the radiationless transition $0 \rightarrow f$ to the level of the final state which is nearest as regards vibrational energy. The

§ To within extremely slow transitions $\upsilon_1 \rightarrow a$ with emission of a photon.

probability of such a transition is defined by the expression (see, for example, Henry and Kasha[54])

$$W_{0f} = \frac{2\pi}{\hbar} L_e^2 F_{0,v_f} \rho_f, \qquad (6)$$

where $L_e = \int \Psi_0 \hat{L} \Psi_f d\tau_e$, Ψ_0 and Ψ_f are adiabatic (without taking into account the interaction with the medium) electronic wave functions of the initial and final states, and F_{0,v_f} is the so called Franck–Condon factor (the square of the overlap integral of the vibrational wave functions of the initial and final states¶).

The multiplier ρ_f is defined as the density of the vibrational levels in the final state. In the absence of the inhomogeneous broadening of the levels, ρ_f differs from zero only within the limits of the level Γ (the Breit-Wigner formula) and the transition $0 \rightarrow f$ can occur only when the levels in wells b_1 and a coincide, i.e. in the presence of resonance. In the case of pronounced broadening it is possible to estimate ρ_f simply as $\rho_f \simeq 1/\hbar\omega_f$. The multiplier ρ_f is then $\hbar\omega_f/\Gamma$ times smaller than at the maximum of the non-broadened resonance line (with a width Γ).

It follows from the properties of the non-adiabatic operator that $\left|\frac{L_e}{\hbar\omega_e}\right| \propto \kappa^3$ where ω_e is the characteristic frequency of the electronic transitions. The Franck–Condon factor depends very markedly (exponentially) on the tunnelling distance $\Delta\vec{d}$ and the mass of the tunnelling group M:

$$F_{0,v_f} \propto f(v_f, \beta) \cdot \exp\left[-\frac{1}{1+\beta^2} \cdot \frac{M\omega_f}{\hbar} \cdot (\Delta d)^2\right], \qquad (7)$$

where $v_f = Q/\hbar\omega_f$, Q is the heat of polymerisation, $\beta = \sqrt{\omega_f/\omega_0}$, and the function f contains Hermitian polynomials.

For estimates, it was assumed that $\omega_e/2\pi \simeq 10^{15}$ s^{-1}, $\omega_f/2\pi c \simeq 1000$ cm^{-1}, and $\omega_0/2\pi c \simeq 100$ cm^{-1}, and $Q \simeq 0.37$ eV (so that $v_f = 3$) was determined experimentally. However, the quantity Δd, which is extremely important for the calculations, remained unknown, because it was impossible to find in the literature data on the geometry of the formaldehyde monomer crystals and even the density of solid formaldehyde at low temperatures is unavailable. However, it is clear that the density of the monomer must be lower than the density of the polymer, because the distance between the neighbouring formaldehyde monomer molecules (planar triangles) $\begin{matrix} H \\ \diagdown \\ C{=}O \\ \diagup \\ H \end{matrix}$ is determined by the relatively large van der Waals radii of the carbon and oxygen atoms and the distance between neighbouring CH_2O groups in the polymer chain is determined by the smaller lengths of the valence bonds; (for example, in polyoxymethylene the C–O bond length is 1.43 Å, which corresponds, for nearly tetrahedral valence angles, to a distance between two neighbouring carbon or oxygen atoms in the polymer chain $d_f \simeq 2.4$ Å).

Extrapolation of the densities of liquid formaldehyde at higher temperatures to the melting point yields $\rho_0 \simeq 1$ g cm^{-3} and the density of polyoxymethylene is $\rho_f \simeq 1.43$ g cm^{-3}. Assuming that $\Delta d \simeq d_f[(\rho_f/\rho_0)^n - 1]$, where $n = 1/3-1$, we obtain a very wide range of values of $\Delta d \simeq 0.3-1$ Å.

The author therefore decided to proceed as follows: the experimental value $W_{0f} \simeq 1/\tau_0 \simeq 10^2$ s^{-1} was adopted and a test was made to discover whether this corresponds to a reasonable value of Δd on the assumption of the tunnelling of the CH_2O group as a whole. Such "reverse" calculation gave $\Delta d \simeq 0.4-0.5$ Å, which is consistent with the above estimates.

The filling of the "vacancy" formed on polymerisation by neighbouring formaldehyde molecules proceeds via a tunnelling resonance transition between zero-point vibrational levels of two neighbouring equivalent wells, $b_{n+1} \rightarrow b_n$ (Fig. 17), i.e. as if by diffusion in the monomer lattice of the cavity formed on polymerisation.

The observed rate of polymerisation is limited either by the fundamental step involving the addition of a new unit to the polymer chain ($0 \rightarrow f$) or by the transport of monomer molecules to the terminal unit ($0 \rightarrow 0$)†. However, it is significant that at very low temperatures both processes have quantum-mechanical mechanisms and are due to tunnelling transitions from the zero-point vibrational level. With increase of temperature, as higher vibrational levels in the initial and final states are filled, the transitions over the barrier begin to play an increasing role and the rate of reaction begins to obey the Arrhenius law (for $M = 30$, $E \simeq 0.1$ eV, and $\Delta d \simeq 0.5$ Å, the boundary between the tunnel and Arrhenius regions is at $T_t \simeq 25$ K).

Thus, although the necessary data are not as yet available for an accurate calculation of the probability of the occurrence at the absolute zero of the chemical reaction involved in the polymerisation of formaldehyde studied by the present author, the estimates obtained are in reasonable agreement with experimental results. Nevertheless, it would also of course be desirable to analyse at least semiquantitatively other possible models and examples of the occurrence of the low-temperature limit to the rates of this and other chemical reactions. At the same time one should bear in mind that, other conditions being equal, the parameter which determines the contribution of the tunnel effect to the observed rate of the process is the product md^2 [or $\sqrt{m}d$—see Eqn. (5) for the characteristic "tunnel temperature"], where m is the mass of the tunnelling species and d the tunnelling distance.

Whereas tunnelling over a distance of tens of angstroms may be typical for an electron at low temperatures, while for a proton the distance is 1–2 Å, for groups with a molecular weight M tunnelling through a barrier with a width $d \simeq 1/\sqrt{M}$ (Å) becomes immeasurably slow and the barrier cannot be overcome in this way. It is therefore possible that the author was lucky to "encounter" formaldehyde, which proved to be one of the extremely rare successful systems for which it is possible to observe and investigate quantitatively the tunnelling of whole molecules or molecular groups.

¶ Eqn. (6) takes into account only one of the complications (mentioned above), which hinder exothermic tunnelling transitions between non-identical potential wells–the necessity for the breakdown of the Franck–Condon principle, i.e. the occurrence of an electron–nucleus interaction. The rate of transfer of the transition energy to the surroundings is not taken into account here, it being assumed that it is much higher than the rate of the transition itself.

† The transport of monomer molecules to the terminal unit (the transition of formaldehyde from well b_{n+1} to well b_n, diffusion of the cavity) can occur, in contrast to chain propagation ($b_1 \rightarrow a$), as a resonance tunnelling transition. Nevertheless, the rate of this transition need not necessarily exceed the rate of intrinsic chain propagation, because, as can be seen from Fig. 17, owing to the exothermic heat of the chemical reaction, the width of the barrier in the $b_1 \rightarrow a$ transition is much smaller than in the $b_{n+1} \rightarrow b_n$ transitions.

It is significant that the present author's findings for the low-temperature polymerisation of formaldehyde constitute to a certain extent models for tunnelling electron transfer between complex biological molecules, already mentioned above, when such transfer requires a conformational change in the biological molecules as an obligatory concomitant process. Although the occurrence of such complex electron transfer has not so far been observed experimentally, it has been postulated[15,16] as an intermediate stage in a process where only the location of the electron is altered but not the geometry of the valence bonds of the oxidant and reductant. Interaction under conditions where the possibility of a non-resonance tunnelling transition of an electron is ensured because it is accompanied by conformational changes in biological macromolecules is illustrated in Fig. 18.[15,16]

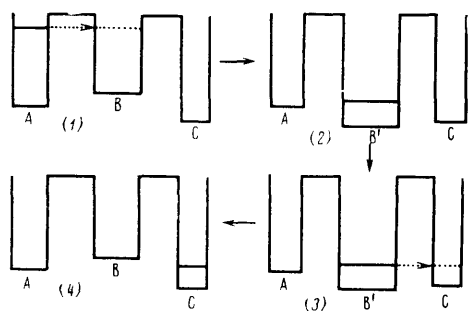

Figure 18. Schematic illustration of electron transfer from the reductant (A) to the oxidant (C) accompanied by conformational transitions of the transferring agent ($B \rightleftharpoons B'$).

Electron transfer from a reductant (potential well A) to an oxidant (well C), occurring with the evolution of energy Q, proceeds only with participation of an intermediate transferring agent. The state of equilibrium of the oxidised form of the transferring molecule is described by the potential well B, while the state of equilibrium of its reduced form is different, owing to the polarisation of the medium, and is described by the potential well B′. When the electron enters well B at the level in resonance with the initial well A, the medium is polarised and the conformational transition $B \rightarrow B'$ takes place, and, when the new electronic level in well B′ is in resonance with a level in well C as a result of this transition, there is a possibility of electron transfer to C and of the reverse conformational transition $B' \rightarrow B$.

Thus the non-resonance electron transition (1) → (4) (Fig. 18) is regarded as the sum of two resonance tunnelling electron transitions: (1) A → B and (3) B → C and two conformational transformations $B_1 \rightarrow B_2'$ and $B_3' \rightarrow B_4$. The main evolution of energy in a set of transitions of this kind occurs in the stage (3) → (4) owing to the conformational transformation of the transferring molecule, which has given up the electron, to the equilibrium configuration for the oxidised form: $B_3' \rightarrow B_4$.

In accordance with the foregoing, the evolved energy Q may be dissipated by the excitation of either phonons or the normal vibrations in the transferring molecules which are fairly strongly linked to the electronic state of the system.

The rate of the combined electronic-conformational transitions should probably tend to a limit on reducing the temperature, as described above for the polymerisation of formaldehyde. Since the processes of the type described should depend on the energy difference between the occupied electronic level of the reductant and the vacant level of the oxidant, it is believed[15,16] that they may be regulated by membrane potentials.

However, the fundamental importance of the above results, the role of the low-temperature tunnelling of not only electrons and protons but also of whole segments of biological molecules or molecular groups, is by no means restricted to this important problem of molecular biology, which is concerned with electronic and conformational transitions.

The detailed study of the low-temperature limit to the rates of chemical reactions and the extension of the reactions investigated towards temperatures still lower than 4 K may be of even wider fundamental significance. For example, the occurrence of chemical reactions at ultralow temperatures makes it necessary to consider seriously whether it would be possible to revive an organism subjected to prolonged freezing under conditions where the influence of external chemical reaction initiators (for example, various types of radiation) is not excluded.

However, another consideration is even more important—near the absolute zero the entropy factors, which are very important in the thermodynamics of chemical reactions, cease to play a role and therefore the equilibria of all reactions are displaced towards exothermic processes, including even those which lead to the formation of highly ordered systems. Furthermore, one should bear in mind the possibility of a kind of autoregulation of the direction of such spontaneous reactions—processes with a relatively small heat evolution (closer to resonance processes) should proceed with greater probability and, as the complexity of the molecules formed increases, the probability of the dissipation of the evolved energy via intramolecular degrees of freedom becomes more pronounced. Admittedly, the rates of reactions near the absolute zero are greatly reduced but, in relation to natural evolutionary processes, one can boldly recall Mayakovskii's words: "eternity awaits both you and me and it would cost us little to waste an hour or two".

It is quite possible that, at the low temperatures in space under the conditions of initiation by cosmic rays, even the most complex molecules, up to proteins, can be reliably formed, although the rate of their formation is extremely slow, and that slow chemical reactions at low and ultralow temperatures, which are, however, clearly directed towards the maximum heat evolution, may play a definite role in the processes involved in chemical and biological evolution. There is a possibility of what one might call a "cold prehistory of life".

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Hyprophosphorous Acid and Its Salts

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The review deals with the analysis of the literature on the synthesis, properties, and applications of hypophosphorous acid and its salts in pharmaceutical practice, for the surface treatment of metals, in analytical chemistry, etc.
The bibliography includes 168 references.

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I. INTRODUCTION

Of the three main acids containing one phosphorous atom in the molecule—phosphoric, phosphorous, and hypophosphorous—the last has been least investigated and is most difficult to synthesise in a high yield; there have also been few studies on its salts (hypophosphites).

Hypophosphites have been attracting attention not only because of their extensive applications as reducing reagents, but also in connection with their possible use for the preparation of various polymeric materials.

Information about the synthesis of hypophosphorous acid and various alkali metal hypophosphites, their structures, and properties, and the conditions governing the formation of their complexes in aqueous and non-aqueous media is presented below.

II. HYPOPHOSPHOROUS ACID: PREPARATION AND PROPERTIES

Pure hypophosphorous acid $H(O_2PH_2)$ consists of white crystals melting at 26.5°C and decomposing above 50°C. Its heat of fusion is 2.4 kcal mole^{-1} [1-4] and the heat of solution of the crystalline acid in water is about −0.18 kcal mole^{-1}.

An interesting laboratory method for the preparation of $H(O_2PH_2)$ involves the oxidation of phosphine (PH_3) in an aqueous suspension of iodine[5]. Phosphine, obtained by the reaction of potassium phosphide with dilute hydrochloric acid, is passed into a flask containing a stirred suspension of iodine until the solution is decolorised. At a reduced pressure (40 mmHg) it is possible to remove hydrogen iodide and water, leaving behind pure $H(O_2PH_2)$. The latter is also formed on slow oxidation of white phosphorus in the presence of water, but its yield is insignificant. When white phosphorus is oxidised by passing moist air over its surface, only 10–12% of the initial amount of phosphorus is converted into $H(O_2PH_2)$.[6]

Hypophosphorous acid is obtained by the decomposition of alkaline earth metal phosphides with water. It is possible to synthesise the acid by treating an aqueous solution of calcium hypophosphite with an equivalent amount of H_2SO_4. A method for the purification of hypophosphorous acid by the recrystallisation of commercial 50% $H(O_2PH_2)$ has been described[7]. The pure acid can be obtained by converting technical sodium hypophosphite into hypophosphorous acid by ion exchange[8].

Hypophosphorous acid is a powerful monobasic acid. According to Kolthoff's data[9-13], its dissociation constant is 8.0×10^{-2}. The fact that hypophosphorous acid is monobasic shows that in this structure the phosphorus has a coordination number of four.

In studies of the kinetics of the oxidation of hypophosphorous acid by halogens by bromine and chlorine (Griffith and McKeown) and by iodine (Griffith et al.)[14-19] it was found that the rate-determining stage of the oxidation is the conversion of the inactive form of hypophosphorous acid $(H_3PO_2)_I$ into the active form $(H_3PO_2)_{II}$. It has been suggested that the $(H_3PO_2)_I$ form is a tautomer with two hydrogen atoms attached to phosphorus, while $(H_3PO_2)_{II}$ contains two hydroxy-groups attached to phosphorus. It is noteworthy that under identical conditions the reaction with chlorine is faster than that with bromine, while the reaction with iodine is slowest.

Fig. 1 presents titration curves for hypophosphorous acid and certain other lower acids of phosphorus. The dissociation constant of $H(O_2PH_2)$ has been compared with the K_{diss} for other acids and it has been shown that these values are consistent with calculated data[20,21].

Table 1 lists the dissociation constants of a number of phosphorus acids.

III. THE STRUCTURE AND PROPERTIES OF THE HYPOPHOSPHITE ION

The structure of the hypophosphite ion has been investigated by X-ray diffraction using ammonium hypophosphite[23,24]. This anion has the form of a distorted tetrahedron two corners of which are occupied by oxygen atoms and the other two by hydrogen atoms, with the phosphorus located in the centre of the tetrahedron. It has been shown that the P–O distance is 1.51 Å, the P–H distance about 1.5 Å, and the O–P–O and H–P–H angles are respectively 120° and 92°.

The structures of magnesium, nickel, and cobalt hypophosphite hexahydrates have been investigated similarly by X-ray diffraction[25,26]. It has been established that in the magnesium salt the $H_2PO_2^-$ anion has a nearly tetrahedral structure with a P–O distance of 1.52 Å and an O–P–O angle of 109°. The observed P–O distances correspond approximately to 0.6 of a π bond per σ bond, which is equivalent to 1.2π bonds per phosphorus atom.

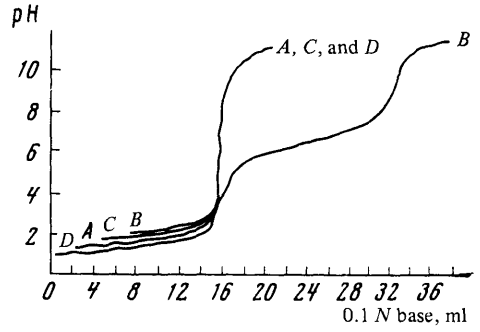

Figure 1. pH titration curves: *A*) for hypophosphorous acid; *B*) for phosphorous acid; *C*) for pyrophosphorous acid; *D*) for hydrochloric acid. The pH values were established relative to standard buffer solutions.

Table 1. Dissociation constants of various phosphorus acids at 20–25°C[22].

Acid	Formula	pK_1	pK_2	pK_3	pK_4
Hypophosphorous	$H^+ + H_2PO_2^-$	1.1	—	—	—
Phosphorous	$2H^+ + HPO_3^{2-}$	1.3	6.7	—	—
Monoethyl phosphite	$H^+ + (RO)HPO_2^-$	0.8	—	—	—
Methylphosphonic	$2H^+ + RPO_3^{2-}$	2.3	7.9	—	—
Propylphosphonic	$2H^+ + RPO_3^{2-}$	2.4	8.2	—	—
Phosphoric	$3H^+ + PO_4^{3-}$	2.1	7.1	12.3	—
Hypophosphoric	$4H^+ + {}^{-2}O_3PPO_3^{2-}$	(2.0)	(2.6)	7.2	10.0
Pyrophosphoric	$4H^+ + {}^{-2}O_3POPO_3^{2-}$	1.0	2.0	6.6	9.6

The ^{31}P NMR spectra[27–30] of hypophosphite solutions reveal 1 : 2 : 1 spin–spin splitting with a between-peak separation of 0.33 G (Fig. 2). Similarly the ^1H NMR spectrum has two peaks corresponding to 1 : 1 spin–spin splitting. This implies that two hydrogen atoms (nuclear spin 1/2) are bound covalently to the phosphorus atom (nuclear spin 1/2) so that, even if their mutual exchange or their exchange with water does occur, these processes are fairly slow (the half-exchange period is of the order of several minutes). According to published data, approximately 95% or more of the free acid or its salts exists in a form where four atoms are linked directly to phosphorus.

The hypophosphite ion has a $[^{31}P]$ spectrum with three peaks of relative intensities 1 : 2 : 1. The phosphite anion contains two peaks of equal intensities in its spectrum and trimethyl phosphite gives rise to nine peaks with the theoretical intensity ratios 1 : 9 : 36 : 84 : 126 : 84 : 36 : 9 : 1. The multiplet structure of the NMR spectra is due to the indirect spin–spin splitting by covalently bound hydrogen atoms.

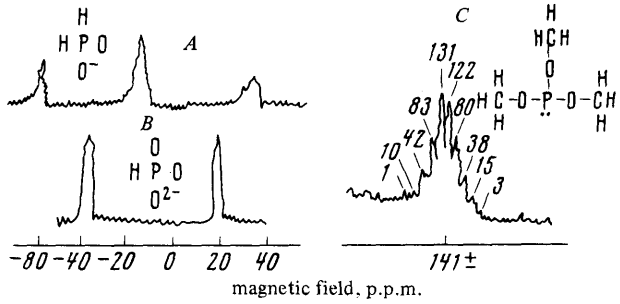

Figure 2. The NMR spectrum of phosphorus in hypophosphite and phosphite anions and in trimethyl phosphite: *A*) hypophosphorous acid; *B*) phosphorous acid; *C*) trimethyl phosphite.

In addition, the Raman spectra of hypophosphorous acid and some of its salts have been investigated[31–37] and it has been shown that the hypophosphite ion has C_{2v} symmetry, attributable to the tetrahedral species $H_2PO_2^-$.

Despite the fact that the acid and its alkali metal and alkaline earth metal salts contain tetracoordinate phosphorus, owing to the equilibrium between tautomeric forms it is possible to displace the equilibrium towards the form with tricoordinate phosphorus. This can be achieved under conditions where an electron acceptor (but not a hydrogen ion) can participate in utilising the free electron pair of the tricoordinate phosphorus atom. Possibly such conditions obtain in addition products or double salts of tin(II) hypophosphite with tin(II) bromide or iodide[38].

The kinetics of the isotope exchange between hypophosphites and water and between hypophosphites and other salts of phosphorus oxyacids have been thoroughly investigated. In earlier studies[39,40] it was stated that the two hydrogen atoms linked directly to the phosphorus atom of the hypophosphite anion are incapable of exchange with the hydrogen atoms of water. However, the latest investigations[41,42] established that this process does occur slowly but at a measurable rate. The rate of substitution of one hydrogen atom of the hypophosphite anion (linked directly to phosphorus) is given by the following equation in which the numerical constants refer to 30.0°C:

$$R = 3.33\,[H^+]\,[H_2PO_2^-] + 2.9\,[H_3PO_2]^2,$$

where R is expressed in litre mole^{-1}h^{-1}. This exchange is believed to be determined by the conversion, mentioned above, of the tautomeric form of the hypophosphite ion into one with tricoordinate phosphorus.

The exchange of oxygen between the hypophosphite ion and water in which it is dissolved has also been studied[43]. It was shown that the half-exchange periods for oxygen in the acid at 40° and 100°C are respectively 70 h and less than 0.2 h. The rate of exchange of oxygen for the sodium salt is so low that it cannot be detected even at 100°C. These data must be compared with the results obtained by the same workers in a study of the exchange of hydrogen

atoms [41,42]. The half-exchange period for hydrogen in $H(O_2PH_2)$ at 25°C is 16 min, while for $Na(O_2PH_2)$ at 100°C the period is 21 h. Possibly the lower rate of oxygen exchange for the sodium salt compared with the acid is a consequence of the presence of a hydrogen bond between the OH groups of the acid and water. This explanation is similar to the theory of electrical conduction proposed by Grotthus [44], according to which the hydrogen atoms joined directly to phosphorus form weaker hydrogen bonds with water than the hydrogen atoms of the OH group.

It has been shown [45-47] that the phosphorus atoms in the hypophosphite ion do not exchange with phosphites and phosphates in either acid or neutral solutions. It is interesting to note that the phosphorus exchange between hypophosphorous and phosphoric acid does not occur in the presence of iodine or iodides, although the oxidation of hypophosphorous acid to phosphorous acid by iodine might give rise to phosphorus exchange at a rate comparable to that of the oxidation-reduction reaction. In mixtures of arsenious and arsenic acids iodine promotes arsenic exchange at a rate which may be predicted from kinetic data for the oxidation-reduction reaction.

The absence of exchange between hypophorous and phosphorous acids in the presence of iodine has been explained on the hypothesis that the process consists of two stages: a slow transition of the inactive form of hypophosphorous acid into the active form and then a rapid irreversible oxidation of the active form by iodine. Thus in the first, reversible stage, the exchange cannot occur, while the second (oxidation-reduction) stage is not accompanied by the exchange owing to its irreversibility. The active form of hypophosphorous acid is probably a tautomeric structure based on tricoordinate phosphorus. This result and data for hydrogen exchange between hypophosphorous acid and water are consistent with the conclusions based on the oxidation of hypophosphites, which will be described below.

Hypophosphorous acid and hypophosphites are readily oxidised. On storage in the cold, the crystals of hypophosphorous acid are stable [7] but contaminated crystals readily decompose at room temperature. The decomposition products are mainly phosphine, phosphorus, phosphoric acid, and hydrogen. Similarly, on vigorous heating, hypophosphites decompose, giving rise to phosphine, red phosphorus, phosphites, phosphates, and possibly other compounds. This type of decomposition is evidently a consequence of self-oxidation-reduction.

The kinetics of the reaction between hypophosphite and hydroxide ions, in which phosphite ions and gaseous hydrogen are formed, have been investigated [48]. The rate equation for this reaction is

$$-\mathrm{d}[H_2PO_2^-]/\mathrm{d}t = K[H_2PO_2^-][OH^-]^2.$$

The rate constant K is approximately 3×10^{-4} min^{-1} at 100°C. It has been suggested that free hydrogen is more readily evolved from the hydroxide ion than from the hypophosphite ion [49].

Hypophosphites also decompose in neutral solutions at a moderate rate, evolving hydrogen in the presence of platinum black, palladium, and copper [48,50-55]. These metals are readily deposited in a colloidal state from solutions of their salts under the influence of sodium hypophosphite. The resulting colloidally dispersed metal then catalyses the decomposition of hypophosphite ions in which hydrogen is evolved.

The study of isotope exchange has shown that the hydrogen evolved from neutral hypophosphite solutions in the presence of metallic catalysts originates from water to the extent of 50%. [56] In this case the catalytic decomposition of the hypophosphite should be consistent with the following chemical equation:

A number of studies have been made of the oxidation of hypophosphites by various oxidising agents. The main product of these reactions is phosphite. The rate of oxidation of sodium hypophosphite in an alkaline medium is approximately three times higher than in a neutral medium: in the former case the completion of the reaction requires 60 min and in the latter 180–200 min. [57] The subsequent oxidation of phosphites to phosphates in an acid solution is much slower. The catalytic effect of freshly deposited nickel on the oxidation of sodium hypophosphite has been investigated [58]. It has been shown that the degree of oxidation of hypophosphite is influenced by temperature, oxidation, time, acidity of the solution, and the amount of catalyst.

As stated above, the kinetics of the oxidation of hypophosphorous acid by halogens have been studied and it has been found that the conversion of the inactive form of hypophosphorous acid $(H_3PO_2)_I$ into the active form $(H_3PO_2)_{II}$ determines the rate of oxidation. The interaction between the active form and halogens takes place after each collision. The constant for the equilibrium between the two forms of hypophosphorous acid has been calculated:

$$K = \frac{[(H_3PO_2)_{II}]}{[(H_3PO_2)_I]} = \frac{K_1}{K_2} \simeq 10^{-12}. \qquad (A)$$

The rate of interconversion of the two forms of hypophosphorous acid has been found to be directly proportional to the hydrogen ion concentration and to determine the rate of oxidation in an acid solution.

The kinetics of the oxidation of hypophosphorous acid by iodate ions have been studied [59-61] and a number of investigations have also been made of the slower reactions with bromates and chlorates [62,63]. The kinetics of the reaction between H_3PO_2 and iodate are close to those of the oxidation of hypophosphites by halogens. However, there are a number of complicating side reactions, for example the interaction of iodine with $H(O_2PH_2)$ and the reaction of phosphorous acid with iodine and iodate. Nevertheless in this case too the rate of oxidation is determined by the stage involving the conversion of $(H_3PO_2)_I$ into $(H_3PO_2)_{II}$. This proved to be the case also in a study of the kinetics of the oxidation of hypophosphite by copper(II) [64-67] and mercury(II) [68-70] salts at moderate concentrations of the oxidant in an acid medium.

The kinetics of the oxidation of hypophosphorous acid in an acid medium by chromate [71], silver [72], iron(III) [73], and arsenate [74] ions have been studied at moderate and high concentrations. It has been found that the type and concentration of oxidising agents have in essence no influence on the rate of the process, which increases appreciably with increasing acidity of the solution. This is reflected by the equation

$$\mathrm{d}[H_3PO_3]/\mathrm{d}t = K[H_3PO_2][H^+],$$

in which K is of the order of 0.24 litre $mole^{-1}min^{-1}$ for all the reactions investigated.

The results of all the kinetic studies are consistent with the claim that the active form of the acid is present in extremely low amounts and that the rate of conversion of

the inactive form into the active form, being slow, determines the rate of the entire reaction under readily realisable experimental conditions.

These results are consistent with NMR data, which have shown that 95% or more of the hypophosphite ions are present in the tautomeric form based on tetracoordinate phosphorus. In conformity with Eqn. (*A*), the fraction of $HP(OH)_2$ in hypophosphorous acid is only 10^{-12} relative to $H_2P(O)(OH)$.

IV. ALKALI METAL AND ALKALINE EARTH METAL HYPOPHOSPHITES

Recently hypophosphites have been used extensively in many countries for chemical nickel plating of metals [75]. There is interest in the application of hypophosphites also in many other branches of industry [76]. In view of the increased requirement for hypophosphites there has been a growth in the amount manufactured. Thus during the period 1955–1960 the production of hypophosphites and hypophosphorous acid in the USA [77] increased from 100 000 lbs to 1 million lbs of the equivalent amount of phosphorus annually. In the USSR in 1967 the production of sodium hypophosphite increased by a factor of several tens compared with 1957.

One of the decisive factors on which the level of requirement of hypophosphites depends is their cost. The existing high cost of hypophosphite in USSR, which is responsible for the high cost of chemical nickel plating [78], is caused, on the one hand, by the low yield (about 36% relative to the phosphorus in the charge) of hypophosphite in the industrial preparation of Na_2HPO_2 via $Ca(H_2PO_2)_2$ and, on the other hand, by the relatively small scale of the industrial production. The low yield of hypophosphite in the reaction of phosphorus with hydroxide ions is due to the fact that the phosphorus in the charge is consumed not only in the formation of the hypophosphite but is also converted into phosphite and passes to the gas phase mainly in the form of phosphine.

The methods for the production of hypophosphites described [79-85] do not allow one to infer the particular factors which influence their yields. The maximum yield of hypophosphite of 70% claimed in a Swiss patent [86] is in no way justified. A low temperature of the synthesis of the solutions is specified in many patents, but its relation to the yield is never discussed. A method has been described [87] for the production of alkali metal hypophosphites in the presence of an aqueous suspension of insoluble alkaline earth metal phosphates, phosphites, sulphates, silicates, and oxalates and also aluminium, magnesium, and silicon oxides and various types of clays as catalysts. These suspensions increase the area of contact between the reactants, which in turn activates the reaction. The mixture is heated above the melting points of phosphorus. A highly pure product is obtained in 90% yield without an excess of the alkali metal or side products.

The method of synthesis of hypophosphites by the reaction of white phosphorus with alkali and alkaline earth metal hydroxides is classical (it was described as early as 1816) and is still used in the industrial production of hypophosphites. Different versions of the main reaction of phosphorus with hydroxides have been described [79,86,88-108]. The yield of the reaction products under laboratory and industrial conditions has been very low, but the increasing interest in hypophosphites has led to the method being patented. The conditions for the preparation of sodium hypophosphite reviewed by Uhlir et al. [82] have been developed on the basis of these patents.

The method used to manufacture sodium hypophosphite adopted in the USSR, consists of two stages. In the first state the reaction of yellow phosphorus with $Ca(OH)_2$ results in the formation of calcium hypophosphite via the reaction

$$8P + 3Ca(OH)_2 + 6H_2O = 3Ca(H_2PO_2)_2 + 2PH_3.$$

In the second stage the resulting calcium hypophosphite is decomposed with sodium carbonate and NaH_2PO_2 is obtained:

$$Ca(H_2PO_2)_2 + Na_2CO_3 = 2NaH_2PO_2 + CaCO_3.$$

The technological parameters of this method are very poor, the degree of utilisation of the initial phosphorus being at best 16–18%. The consumption of lime is four times the stoichiometric amount. The rate of synthesis of calcium hypophosphite is low, the concentration of the resulting solutions is 7–8 g litre^{-1}, and the consumption of steam in the evaporation of such solutions is high. The effluent gases from the synthesis (PH_3) are not used. In the method adopted the most important stage, responsible for the low efficiency of the entire industrial cycle, is the synthesis of calcium hypophosphite.

Soviet scientists developed recently a number of improvements to this method leading to a higher yield and a faster process. The existing view that the reaction between yellow phosphorus and calcium hydroxide in an aqueous medium is "sluggish" proved to be incorrect; an increase in the specific surface of phosphorus accelerates the synthesis by a factor of several powers of ten. Above 90–93 °C, the rate of reaction increases very rapidly and near 100 °C the process is completed in 2–3 min in the presence of a high specific surface.

Under these conditions, it is possible to obtain solutions containing 12–13% of calcium hypophosphite. The attainment of high rates and high hypophosphite concentrations during the synthesis makes it possible to reduce by a factor of 15 the consumption of steam in the evaporation of the solutions and to reduce sharply the volume of the reactors. The possibility of a considerable decrease of the consumption of calcium hydroxide has been established. Instead of a 400% excess, one can use an excess of approximately 25% relative to stoichiometry. The employment of closed reactors-emulsifiers makes it possible to utilise the PH_3 obtained in the synthesis by its combustion to P_2O_5 with subsequent synthesis of phosphoric acid, which increases the degree of utilisation of phosphorus to 75–80%.

The following conditions for the synthesis in reactors-emulsifiers must be regarded as optimal: the temperature of synthesis 90–93 °C and molar proportions of phosphorus and lime (P : CaO) of 1 : 0.45, which corresponds to an approximately 25% excess of lime. The amount of water introduced into the synthesis is calculated to give 12–13% solutions.

Morgunova and Averbukh [109] made a detailed study of the synthesis of sodium hypophosphite from (1) yellow phosphorus and sodium hydroxide, (2) yellow phosphorus, calcium hydroxide, and sodium carbonate, (3) yellow phosphorus, sodium hydroxide, and calcium hydroxide, (4) yellow phosphorus, barium hydroxide, and sodium carbonate, and (5) yellow phosphorus, sodium hydroxide, and barium hydroxide. During their investigations, they established that an increase of the yield of sodium hypophosphite to 55–59% of the phosphorus in the charge can be ensured by preparing the sodium hypophosphite solution in a single stage by the reaction of phosphorus with hydroxide

ions in the presence of both Na^+ ions alone and in the joint presence of Na^+ and Ca^{2+}. When Ca^{2+} ions are replaced by Ba^{2+}, the yield falls. The overall amount of hydroxide ions introduced into the process, which can ensure the complete utilisation of the phosphorus in the charge, should be not less than 1.0–0.9 mole per gram-atom of phosphorus. A decrease of the content of phosphite formed during the synthesis is achieved by precipitating it in the form of insoluble alkaline earth metal phosphites. The amount of alkaline earth metal required to precipitate the phosphite may be 0.25–0.30 mole per gram-atom of phosphorus, which is determined by the amount of phosphite formed in the synthesis.

In the synthesis of sodium hypophosphites in the presence of hydroxide ions introduced as the alkaline earth metal hydroxide, Na^+ ions can be introduced both as the hydroxide and as the carbonate. When sodium ions are added as the carbonate, the required amount of hydroxide ions must be introduced in the form of the alkaline earth metal hydroxide. The amounts of reactants in the charge should ensure the molar ratios $P : Na^+ : Ca^{2+}(\text{or } Ba^{2+}) : OH^- = 1 : 0.50–0.60 : 0.25–0.30 : 0.90–1.0$.

V. THE MECHANISM OF THE SYNTHESIS OF HYPOPHOSPHITES IN SOLUTION

There exist various views on the relation between the composition of the gas phase and that of the products formed in the synthesis of hypophosphites in solution[80]. Some investigators believe that the amount of hydrogen evolved is proportional to the amount of phosphite formed in the oxidation of hypophosphite:

$$P_4 + 3OH^- + 3H_2O \rightarrow 3H_2PO_2^- + PH_3; \quad (1)$$

$$H_2PO_2^- + OH^- \rightarrow HPO_3^{2-} + H_2 \uparrow, \quad (2)$$

while others state that hydrogen is formed in an amount proportional to the amount of hypophosphite.

Reactions which agree best with practical results according to the authors have been put forward[81]:

$$P_4 + 4OH^- + 4H_2O \rightarrow 4H_2PO_2^- + 2H_2; \quad (3)$$

$$P_4 + 4OH^- + 2H_2O \rightarrow 2HPO_3^{2-} + 2PH_3. \quad (4)$$

Different amounts of phosphite and phosphine are formed by reactions (3) and (4). There exist also other views on the pathways followed in the formation of phosphites and hydrogen[80], but the presence of both components in the gaseous mixture is never denied. According to one investigation[82] the synthesis of sodium hypophosphite involves other reactions, apart from those quoted above, in which molecular hydrogen and diphosphine are formed:

$$3P_4 + 8OH^- + 8H_2O \rightarrow 8H_2PO_2^- + P_2H_4; \quad (5)$$

$$H_2PO_2^- + 2OH^- \rightarrow PO_4^{3-} + 2H_2; \quad (6)$$

$$15P_2H_4 \rightarrow P_{12}H_6 + 18PH_3. \quad (7)$$

In his most complete and latest monograph on phosphorus, Van Wazer[110] quotes the same reactions as Tsuboi[31].

Soviet investigators[111] made a fairly detailed study of the mechanism of the synthesis of hypophosphite in solution. They showed that, when phosphorus interacts with hydroxide ions, hypophosphite and phosphite are formed simultaneously. Presumably both hydrogen and phosphine can be evolved under these conditions.

Morgunova and Averbukh quote in their paper[111] the free energies of some of the reactions calculated from Latimer's data[112] (Table 2). All the reactions listed in the Table, except the last, are thermodynamically probable. In order to determine which reactions actually occur, the authors studied the composition of the gas phase in the synthesis of hypophosphite solutions.

Table 2. The free energies of certain reactions (Latimer's data[112]).

No. of reaction	Reaction	Free energy, kJ
1	$P_4 + 3OH^- + 3H_2O \rightarrow 3H_2PO_2^- + PH_3$	−336.0
2	$H_2PO_2^- + OH^- \rightarrow HPO_3^{2-} + H_2$	−142.8
3	$P_4 + 4OH^- + 4H_2O \rightarrow 4H_2PO_2^- + 2H_2$	−472.2
4	$P_4 + 4OH^- + 2H_2O \rightarrow 2HPO_3^{2-} + 2PH_3$	−485.2
8	$P_4 + 4OH^- + 8H_2O \rightarrow 4HPO_3^{2-} + 8H_2$	−722.8
9	$P_4 + 6H_2O \rightarrow 3H_3PO_2 + PH_3$	−126.4
10	$H_2PO_2^- + 2OH^- \rightarrow PO_4^{3-} + 2H_2$	−199.5
11	$HPO_3^{2-} + 3OH^- \rightarrow PO_4^{3-} + 2H_2O$	−217.1
12	$3H_3PO_2 \rightarrow PH_3 + 3H_3PO_3$	−125.5
13	$H_3PO_2 + H_2O \rightarrow H_3PO_3 + H_2$	−96.6
14	$4H_3PO_3 \rightarrow PH_3 + 3H_3PO_4$	+3.8

Their investigations showed that the composition of the gas phase depends on which hypophosphite is synthesised. In the synthesis of calcium hypophosphite the gas phase contains more phosphine than hydrogen. Three times as much PH_3 as H_2 is always present in the gas phase. A clear-cut dependence of the change in the composition of the gas phase on time has not been observed.

In the synthesis of sodium hypophosphite the content of hydrogen is approximately three times greater than that of PH_3. The $H_2 : PH_3$ ratio then decreases, reaching in some cases approximately 0.6 at the end of the synthesis. The average $H_2 : PH_3$ and hypophosphite : phosphite ratios in the synthesis of calcium hypophosphite are 0.3 and about 1.4, while in the synthesis of sodium hypophosphite from yellow phosphorus and NaOH the ratios are 1.8 and 3.5 respectively.

Table 3. The contributions of reactions (1), (4), (3), and (8) to the synthesis (%).

Sodium hypophosphite				Calcium hypophosphite			
(1)	(4)	(3)	(8)	(1)	(4)	(3)	(8)
—	35.7	64.3	—	impossible			
88.3	—	—	16.7	impossible			
impossible				26.7	53.4	19.9	—
80.6	—	1.6	17.8	impossible			
—	31.6	63.5	0.4	impossible			

Possible combinations of reactions which ensure the formation of both hydrogen and phosphine in the above proportions and which are the most probable on thermodynamic grounds [reactions (1), (4), (3), and (8) in Table 2] have been elucidated. The possible combinations of reactions in the synthesis of hypophosphites are indicated in Table 3, which shows that the combination of reactions

(4) and (3) is feasible only in the synthesis of sodium hypophosphite solutions and is impossible in the synthesis of calcium hypophosphite. This has also been pointed out in other investigations[82,112]. The synthesis of hypophosphites may involve the simultaneous occurrence of reactions (1), (4), (3), and (8) with formation of hypophosphite. Apart from phosphine, the gas phase contains diphosphine, which causes the self-ignition of the evolved gases in air. Furthermore, a certain amount of elemental phosphorus passes to the gas phase.

VI. HYPOPHOSPHITES AND THEIR CLASSIFICATION

The available literature data are mainly concerned with studies on alkali metal phosphites. The following alkali metal hypophosphites are known[80]: $Li(O_2PH_2).H_2O$, $K(O_2PH_2)$, $Na(O_2PH_2).H_2O$, and the ammonium salts $(NH_4)(O_2PH_2)$ and $(NH_3OH)(O_2PH_2)$. They are all readily soluble in water. However, there are no reliable data for their solubilities[114] except for the solubilities of the sodium salt in two glycols. At 25°C $Na(O_2PH_2)$ dissolves in an amount of 33.01 g in 100 g of ethylene glycol and 9.70 g in 100 g of propylene glycol. The heats of solution of the sodium, ammonium, calcium, and barium salts have been determined by Bright and Carson[113].

The following Group II metal hypophosphites are known[80]: $Mg(O_2PH_2).6H_2O$, $Ca(O_2PH_2)_2$, $Sr(O_2PH_2)_2$, $Ba(O_2PH_2)_2$, and $Ba(O_2PH_2)_2.H_2O$. These salts are also extremely soluble in water, the solubilities of $Ca(O_2PH_2)_2$ and $Ba(O_2PH_2)_2$ at room temperature being respectively 17 and 29 g per 100 g of water.

As a rule, other metal hypophosphites are obtained by the reaction of the metal oxide or hydroxide with hypophosphorous acid. In many cases, when the metal can be readily reduced, an oxidation-reduction takes place instead of the formation of the salt. Such processes occur, for example, when copper and silver oxides are used. However, salts such as copper hypophosphite can sometimes be obtained by cooling or by rapid salting-out with alcohol[114].

The physical properties and solubilities of some hypophosphites which we have found in the literature are compiled in Table 4.

Myants and Matrosov[115] studied the infrared spectra of metal hypophosphites and carried out calculations on various vibrational models. The salts were obtained by the double decomposition of the metal with barium and potassium hypophosphites. Drying in a Fisher pistol over P_2O_5 at 77°C (the salts decomposed at a higher temperature) resulted in only a partial loss of the water of crystallisation. The starting materials and the compositions of the salts obtained are listed in Table 5.

Table 5. The hypophosphites which have been synthesised and investigated.

Starting materials	Composition of resulting salt	Composition of salt after drying
$(NH_4)_2SO_4$ and $Ba(H_2PO_2)_2$	$NH_4H_2PO_2$	$NH_4H_2PO_2$
Li_2SO_4 and $Ba(H_2PO_2)_2$	$LiH_2PO_2 \cdot H_2O$	LiH_2PO_2
Na_2SO_4 and $Ba(H_2PO_2)_2$	$NaH_2PO_2 \cdot \frac{1}{3} H_2O$	NaH_2PO_2
$MgSO_4 \cdot 7H_2O$ and $Ba(H_2PO_2)_2$	$Mg(H_2PO_2)_2 \cdot 6H_2O$	$Mg(H_2PO_2)_2 \cdot H_2O$
$ZnSO_4 \cdot 7H_2O$ and $Ba(H_2PO_2)_2$	$Zn(H_2PO_2)_2 \cdot \frac{1}{2} H_2O$	$Zn(H_2PO_2)_2 \cdot \frac{1}{2} H_2O$
$CdSO_4 \cdot \frac{8}{3} H_2O$ and $Ba(H_2PO_2)_2$	$Cd(H_2PO_2)_2 \cdot 2H_2O$	$Cd(H_2PO_2)_2 \cdot H_2O$
Tl_2SO_4 and $Ba(H_2PO_2)_2$	TlH_2PO_2	TlH_2PO_2
$Th(NO_3)_4$ and KH_2PO_2	$Th(H_2PO_2)_4 \cdot 3H_2O$	$Th(H_2PO_2)_4 \cdot 3H_2O$
$Pb(NO_3)_2$ and KH_2PO_2	$Pb(H_2PO_2)_2 \cdot H_2O$	$Pb(H_2PO_2)_2 \cdot H_2O$
$MnSO_4 \cdot 7H_2O$ and $Ba(H_2PO_2)_2$	$Mn(H_2PO_2)_2 \cdot 3H_2O$	$Mn(H_2PO_2)_2 \cdot 2H_2O$
$Fe_2(SO_4)_3 \cdot 9H_2O$ and $Ba(H_2PO_2)_2$	$Fe(H_2PO_2)_3 \cdot H_2O$	$Fe(H_2PO_2)_3$
$NiSO_4$ and $Ba(H_2PO_2)_2$	$Ni(H_2PO_2)_2 \cdot 6H_2O$	$Ni(H_2PO_2)_2$
$CoCO_3$ and H_3PO_2	$Co(H_2PO_2)_2 \cdot 2H_2O$	$Co(H_2PO_2)_2 \cdot H_2O$

Despite the wide variety of metals, the salts investigated have mainly similar spectra. The infrared spectra of the salts in the solid state (KBr discs) have been investigated in the range 400–3000 cm^{-1} on IKS-14 apparatus; the spectra of aqueous solutions have also been obtained for salts which are readily soluble in water. The presence of two bands due to the vibrations of the P–O bond (antisymmetric at 1115–1200 cm^{-1} and symmetric at 1020–1060 cm^{-1}) is characteristic of all the salts; this shows that the structure of the anion with equalised PO

Table 4. Physical properties of certain hypophosphites.

Formula	Mol.wt.	Colour, crystalline form, refractive index	Density	B.p., °C	M.p., °C	Solubility, g/100 g of solvent		
						in cold water	in hot water	in other solvents
$NH_4H_2PO_2$	83.03	colourless, orthorhombic	2.515	240*	200	sol.	v.sol.	soluble in alcohol NH_3, insoluble in acetone
$Ba(H_2PO_2)_2 \cdot H_2O$	285.33	white lustrous, polyhedral	2.87(10°)	—	**	28.6	33.3	moderately sol. in alcohol
$Fe(H_2PO_2)_3$	250.81	pale grey, porous	—	—	**	0.043(25°)	0.083(100°)	sol. in citrate salt soln.
KH_2PO_2	104.09	white, deliquescent, hexagonal	—	—	**	v.sol.	v.sol.	sol. in chloroform (11.1 at 25°C) and very slightly sol. in abs. alcohol
$Ca(H_2PO_2)_2$	170.05	pale grey, polyhedral	—	—	**	15.4(25°)	12.5(100°)	insol. in alcohol
$Mg(H_2PO_2)_2 \cdot 6H_2O$	262.39	white cryst.	—	—	—	20	—	insol. in alcohol and ether
$Mn(H_2PO_2)_2 \cdot H_2O$	202.93	pink cryst.	—	150	—	12.5	16.7	insol. in alcohol
$NaH_2PO_2 \cdot H_2O$	155.99	colourless, polyhedral	—	200	—	100(25°)	667(100°)	v. sol. in alcohol and slightly sol. in NH_3
$Ni(H_2PO_2)_2 \cdot 6H_2O$	296.80	green, cubic	1.82(20°)	—	100*	sol.	—	—
H_3PO_2	63.98	cryst.	—	—	—	reacts	reacts	—
$Zn(H_2PO_2)_2 \cdot H_2O$	213.36	colourless, hygr., cryst.	—	—	—	sol.	—	reacts with alkali

* Decomposition temperature.
** Compound decomposes.

bonds persists in all cases. The bands in the region of 1150–1160, 1080, and 810 cm^{-1}, which are associated with the variation of the angles α and γ in the phosphorus tetrahedron, remain at the same wavenumbers in the spectra of all the salts. For salts which exist in the form of hydrates, the intense bands in the range 2300–2500 cm^{-1} correspond to the vibration frequency of the water of crystallisation involved in strong hydrogen bonding.

The spectra of the alkali metal salts are similar and can be satisfactorily interpreted in terms of the ionic model. Furthermore, they resemble the spectrum of the tetraalkylammonium salt, which is ionic. This makes it possible to attribute an ionic structure to them.

The spectra of a number of the metal salts show changes relative to those of the alkali metal salts (the spectra of the anion), which depend on the nature of the metal: (1) new bands appear in the range 400–600 cm^{-1}; (2) the P–O bond vibration frequencies exhibit an appreciable bathochromic shift. These changes suggest the formation of the M–O coordinate bond and the similarity of the spectra of all the salts (including the alkali metal salts) shows that the equalisation of the PO bonds persists in all cases.

In the spectra of $Mg(H_2PO_2)_2$, $Ca(H_2PO_2)_2$, and TlH_2PO_2 the shift of the P–O vibration frequencies is slight, which demonstrates that the interaction of the metal with the oxygen atoms of the anion is weak. These salts have a nearly ionic structure. A chain model, in which the metal is linked to one of the oxygen atoms of each anion forming the coordination sphere of the metal, has been proposed for other salts with an appreciable amount of covalent character.

Thallium hypophosphite has been obtained and investigated in detail[8]. The authors concluded that the following method is most suitable for the preparation of large amounts of the pure salt: a TlOH solution is prepared by shaking thin plates of metallic thallium with an 80% excess of water, the mixture being simultaneously bubbled with oxygen. The solution is then filtered and saturated with carbon dioxide; after partial evaporation and cooling, Tl_2CO_3 precipitates and may be recrystallised from water. The thallium carbonate crystals are treated with hypophosphorous acid, and the resulting solution is filtered and concentrated *in vacuo*. A large amount of n-propyl or isopropyl alcohol (3 litres of the alcohol per 100 ml of the saturated salt solution) is added to the residual solution and the resulting mixture is cooled at 5°C for one week. The white acicular crystals formed are washed with fresh isopropyl alcohol and the product is then dried in a vacuum desiccator. The melting point of TlH_2PO_2 has been determined as 114°C. The salt is usually seen to undergo a slight decomposition near its melting point. On heating, thallium hypophosphite gradually blackens. Heating for 6–7 h at 95°C is needed before blackening begins. It has been suggested[8] that under these conditions TlH_2PO_2 is slowly oxidised by atmospheric oxygen to thallium phosphite TlH_2PO_3. Thallium hypophosphite is sensitive to light: the same black colour appears in sunlight as on heating.

The existence of the complex Tl^{3+}–$H_2PO_2^-$ is doubtful[116]; the only evidence for it is the properties of the $H_2PO_2^-$ ligand, which forms complexes with other metals. The following mechanism has been proposed for the formation of the complex of $H_2PO_2^-$ with Tl^{3+} before the oxidation stage:

$$Tl^{3+} + H_3PO_2 \rightleftarrows (TlH_3PO_2)^{3+}$$
$$(TlH_3PO_2)^{3+} + H_2O \rightarrow Tl^+ + H_3PO_3 + 2H^+.$$

The decomposition of the complex is not a simple process; it involves the addition of an oxygen atom to form H_3PO_3, which takes place by the substitution of one hydrogen atom linked directly to phosphorus by an OH group of water.

The properties of anhydrous $Co(H_2PO_2)_2$, $Zn(H_2PO_2)_2$, $Fe(H_2PO_2)_2$, $Cu(H_2PO_2)_2$, and $Ni(H_2PO_2)_2$ have been described[117]. The first two compounds were obtained by crystallisation from aqueous solutions. The salts $Fe(H_2PO_2)_2$ and $Cu(H_2PO_2)_2$ have been prepared by precipitation from acetone solution. Iron hypophosphite is a pale-blue powder insoluble in water. Copper hypophosphite is unstable at room temperature and decomposes with formation of metallic copper a few minutes after precipitation.

Nickel hypophosphite, consisting of an amorphous yellow powder, has been prepared by dehydrating the hexahydrate or by precipitation from acetone solution and dehydration in the presence of P_2O_5.[117] The behaviour of cobalt, zinc, iron, copper, and nickel hypophosphites in relation to anhydrous pyridine has been studied. Cobalt and zinc hypophosphites form the readily crystallising compounds $Co(H_2PO_2)_2Py_2$ and $Zn(H_2PO_2)_2Py_2$. They lose pyridine at 20°C, being reconverted into the corresponding hypophosphites.

It has been found that the interaction of M^{2+} (M = Cu, Co, or Ni) and $H_2PO_2^-$ in aqueous solution at 19° ± 2°C, an ionic strength of 3 ($NaClO_4$), and pH 3.7–3.9 results in the formation of relatively unstable hypophosphite complexes[118] The composition of cobalt and nickel hypophosphites with the ratio $M^{2+}:H_2PO_4^- = 1:1$ has been established by the method of continuous variations. The equilibrium constant for the reaction $M^{2+}H_2PO_2^- \rightleftharpoons MH_2PO_2^+$ (for M = Co) has been calculated as 0.82 ± 0.09.[119]

The synthesis of aluminium hypophosphite by two methods has been described[120]. One of them reduces to heating aluminium hydroxide or an aluminium salt solution with 50% H_3PO_2 at 80–90°C for 1 h with subsequent slow precipitation of $Al(H_2PO_2)_3$. The second method involves heating an aluminium salt with sodium hypophosphite, the precipitation being even slower than in the first method. $Al(H_2PO_2)_3$ is insoluble in water and H_3PO_2. It is soluble in warm sodium hydroxide solution, dilute H_2SO_4, and dilute and concentrated HCl. On heating, aluminium hypophosphite decomposes, without fusion, at approximately 220°C with evolution of phosphine and the formation of a reddish-brown deposit. The conditions under which hypophosphorous acid might reduce aluminium compounds to the metal have not been found.

Scandium, yttrium, and lanthanum hypophosphites $R(H_2PO_2)_3$ have been obtained by the interaction of the hydroxides of the first two elements and of $La_2(CO_3)_3$ with hypophosphorous acid[121]. The resulting hypophosphites are crystalline substances insoluble in water and organic solvents. They crystallise in a system with low symmetry. Scandium hypophosphite decomposes *in vacuo* at 350°C, yttrium hypophosphite at 450°C, and lanthanum hypophosphite at 300–350°C. The infrared spectra of scandium, yttrium, and lanthanum hypophosphites have sharp maxima. The spectra recorded in the range 400–3000 cm^{-1} are mainly those of the anions. The influence of the cations on the spectrum is manifested mainly in the range 400–500 cm^{-1}.

The anhydrous lanthanide hypophosphites having the composition $R(H_2PO_3)_3$ and the double hypophosphites $CeR(H_2PO_2)_6$, where R = Er, Tm, Yb, or Lu, have been synthesised[122,123]. The former are crystalline substances with the colour characteristic of the lanthanide ion, which, however, is less intense than that of the nitrates, chlorides,

and other salts. The results of heating to 105–108°C showed that they do not contain water of crystallisation. Heavy lanthanide hypophosphites are less soluble in water than light lanthanide hypophosphites. They tend to form supersaturated solutions, this tendency being most marked for the light lanthanides.

Lanthanum hypophosphite $La(H_2PO_2)_3.H_2O$ and europium hypophosphite $Eu(H_2PO_2)_3.H_2O$ have been investigated by X-ray diffraction[124] and it has been shown that the chemical properties of these compounds in solutions are somewhat different.

Praseodymium hypophosphite $Pr(H_2PO_2)_3$ crystallises in the form of green prisms when a 1% of H_3PO_2 solution is neutralised with praseodymium oxide and then evaporated on a water bath. The salt is fairly sparingly soluble in water.

The double hypophosphites $CeR(H_2PO_2)_6$, where R = Er, Tm, Yb, or Lu, have been analysed chemically and their thermal decomposition has been studied[123]. It has been established that the decomposition takes place instantaneously in the temperature range 300–370°C. The decomposition products are oxidised in the range 440–600°C.

VII. METAL HYPOPHOSPHITE COMPLEXES

The existence in solution of cationic complexes $MH_2PO_2^{2+}$ formed by lanthanide and hypophosphite ions has been confirmed spectrophotometrically for praseodymium, neodymium, and erbium. The equilibrium constants and the formation constants of the complexes have been calculated[125]. The interaction of lanthanide ions with hypophosphorous acid was studied using an SF-10 recording spectrophotometer. The absorption spectra of solutions of praseodymium(III), neodymium(III), and erbium(III) complexes were recorded in the ranges 420–505, 490–615, and 500–560 nm respectively 10 min after mixing the solutions (this time interval was sufficient for equilibration). The absorption spectra do not change in the course of the next 2–3 h, but for an $H_3PO_2 : M^{2+}$ ratio exceeding 8 or at pH 3.0 a precipitate is formed.

The optical densities of solutions of the hypophosphite complexes at the absorption band maxima of the Pr^{3+} and Nd^{3+} ions are lower and in the case of Er^{3+} higher than the optical densities D_{chl} of solutions of their chlorides. The Pr^{3+} and Nd^{3+} absorption band maxima undergo bathochromic or hypsochromic shifts. The split erbium band has maxima at 522.5 and 519 nm. A study of the influence of the pH on ΔD at the absorption band maxima showed that the formation of lanthanide complexes of $H_2PO_4^-$ begins at a pH greater than 1, reaching a maximum at pH 2.5 for praseodymium and neodymium and at 1.6 for erbium. When the pH of solutions of the praseodymium and neodymium complexes is greater than 6.5 and that of the erbium complex greater than 3, precipitates are gradually deposited from the solutions at a rate which is higher the higher the pH and the greater the $H_2PO_2^- : M^{3+}$ ratio.

The compositions of the complexes have been investigated[125] spectrophotometrically by the isomolar series method and by the restricted logarithmic method. Experiments were performed at pH 2.9–3.4 where the difference between the optical densities of solutions of the complexes reaches a maximum. The formation of highly dissociated complexes with the probable component ratio $H_3PO_2^- : M^{3+} = 1 : 1$ has been established.

The reaction between lanthanide ions and hypophosphorous acid can be represented by the equation

$$M^{3+} + H_3PO_2 \rightleftarrows MH_2PO_2^{2+} + H^+.$$

The values of $\lg K_{eq}$ and $\lg K_{form}$ obtained are listed in Table 6, which shows that those for the praseodymium, neodymium, and erbium complexes differ insignificantly from one another.

Table 6. The logarithms of the equilibrium constants and the formation constants of lanthanide complexes of H_3PO_2.

Complex	K_{eq}	K_{form}
$PrH_2PO_2^{2+}$	0.23±0.03	1.33±0.03
$NdH_2PO_2^{2+}$	0.00±0.04	1.10±0.04
$ErH_2PO_2^{2+}$	0.37±0.03	1.47±0.03

The kinetics of the formation of iron[126] and chromium[127] monohypophosphite complexes have been studied. The existence of the complexes $CrH_2PO_2^{2+}$ and $Fe(H_2PO_2)_2^{2+}$ has been confirmed and their stability constants have been determined. The preparation of tin(IV) hypophosphite has been described[128]. A saturated solution of SnO in H_3PO_2 was saturated with oxygen until colourless $Sn(H_2PO_2)_4$ crystals formed, this being the first example of a solid compound containing tin(IV) and an anion with a high reduction potential. The possibility of the formation of zirconium and hafnium hypophosphite complexes has been studied. It has been shown by ion exchange[129] that the anionic complexes $[Zr(H_2PO_2)_6]^{2-}$ and $[Hf(H_2PO_2)_6]^{2-}$ are formed when hydrated zirconium(IV) and hafnium(IV) oxides are dissolved in an aqueous H_3PO_2 solution (maximum concentration 0.3 N).

The formation of insoluble compounds of the type $M[Zr(H_2PO_2)_6]$ and $M[Hf(H_2PO_2)_6]$ when bivalent metal salts are added (M = Mg, Ca, Mn, Co, Ni, Fe, Zn, or Cd) is of interest. It has been shown[129] that these insoluble bivalent metal hypophosphitozirconates and hypophosphitohafnates do not contain water and decompose at 210–300°C. Apart from the calcium salt, they are all isomorphous. According to infrared spectroscopic data, both terminal and bridging H_2PO_2 groups have been detected in $M[Zr(H_2PO_2)_6]$ and $M[Hf(H_2PO_2)_6]$. Consequently the hypophosphitozirconates and hypophosphitohafnates are polycondensed complexes. It has been found[130] that H_3PO_2 forms with molybdenum(VI) a complex having a high optical density at 400 nm whatever the acid concentration, while the complex with PO_4^{3-} is not formed at a solution acidity of about 1.6 N. A spectrophotometric method for the determination of hypophosphite in the presence of phosphates has been developed on this basis.

Like phosphites, hypophosphites form addition products[131] with hydrogen halides (HCl, HBr, and HI). Whereas phosphates can combine with three molecules of the hydrogen halide, hypophosphites and phosphites can combine with two molecules. A typical compound of this type is $Cd(H_2PO_2)_2.2HCl$. In these compounds the hydrogen halide is linked to the hypophosphite molecule, similarly to water in hydrates, i.e. is coordinated to the metal ion.

Interesting germanium(II) complexes have been described[132]: $Ge(H_2PO_2)_2.GeCl_2$ and $3Ge(H_2PO_2)_2.GeBr_2$. The former salt (m.p. 124°C) was synthesised by heating

activated germanium oxide, obtained by dissolving the normal oxide in alkali and reprecipitating it with 6 *N* HCl and 50% H_3PO_2 in the course of 30 min. After allowing the mixture to stand for 12 h, the crystals were separated, washed with dilute H_3PO_2 and absolute alcohol, and dried *in vacuo* at room temperature. The latter salt (m.p. 129°C) was obtained using GeO, 35% HBr, and 50% H_3PO_2. Crystals separated on slow cooling. The compounds obtained are extremely stable in air, but are hydrolysed in water, forming germanium hydroxide.

When germanium dioxide is heated with H_3PO_2, it is reduced, dissolving with formation of a yellow-green solution. This behaviour is the opposite to that of SnO_2, which, although soluble in H_3PO_2, is not reduced to the bivalent state in the absence of HCl.[132] Everest[133] states that the double salts $Sn(H_2PO_2)_4.SnCl_4$ and $Sn(H_2PO_2)_2.SnCl_2$ exist.

VIII. REDUCING PROPERTIES OF THE HYPOPHOSPHITE ION

Many studies have been made on the reducing properties of hypophosphite ions. Pyrolysis of NaH_2PO_2 in the presence of LiH (molar ratio 1 : 22) or LiOH (molar ratio 1 : 5) has been investigated in the range 210–250°C.[132] The possibility of the following reactions has been suggested:

$$NaH_2PO_2 + LiH \rightarrow NaHPO_2 + Li + H_2 , \quad (15)$$

$$NaH_2PO_2 + 2LiH \rightarrow NaPO_2 + 2Li + 2H_2 , \quad (16)$$

$$6NaH_2PO_2 + 3LiH \rightarrow 2Na_3PO_4 + P_4H_4O + 3LiOH + H_2 , \quad (17)$$

$$NaH_2PO_2 + 4LiH \rightarrow PLi_3 + NaOH + LiOH + 3H_2 , \quad (18)$$

$$NaH_2PO_2 + LiOH \rightarrow NaLiHPO_3 + H_2 , \quad (19)$$

$$NaPO_2 + LiOH \rightarrow NaLiHPO_3 , \quad (20)$$

$$NaH_2PO_2 + 3LiOH \rightarrow NaLi_3H_2PO_4 + 2H_2 , \quad (21)$$

$$2NaH_2PO_4 \rightarrow PH_3 + Na_2HPO_4. \quad (22)$$

The compound P_4H_4O, obtained in reaction (17), is a mixture of red polymeric products. It is insoluble in water, acids, and organic solvents. It has been shown[134] that P_4H_4O is satisfactorily described by the formula $(P_4H_4O)_n$. The possible structure of $(P_4H_4O)_n$ has been considered on the basis of the infrared spectra and possible structural formulae, containing the P–P bond, have been put forward. It has been suggested that P–O–P or –P=O and HO–P– linkages may be formed. P_4H_4O is not formed in the interaction of NaH_2PO_2 with LiOH.

The reduction of $K_3[Co(CN)_6]$ by hypophosphorous acid in 1 *N* HCl solution in an atmosphere of nitrogen, resulting in the formation of $Co(CN)_2.2H_2O$, has been studied[135]. The hypothesis that the reduction reaction proceeds via the intermediate complexes $[Co(CN)_5.OP(O)H_2]^{4-}$ or $[(CN)_5CoOPH_2OCo(CN)_5]_n$ has been confirmed by infrared spectra, which contain absorption bands characteristic of the P–O and P–H groups.

The high reducing capacity of the hypophosphite ion constitutes the basis of many methods for its determination. Thus a procedure has been developed[135] for potentiometric titration with vanadate of hypophosphite and phosphite in their mixtures, based on the oxidation of $H_2PO_2^-$ to PO_4^{3-} (via HPO_3^{2-}) by vanadate in the presence of a silver salt; in the absence of silver, phosphite is not oxidised to PO_4^{3-}.

A volumetric method for the determination of hypophosphite with iodine has been described[137]. It consists in the oxidation of hypophosphite to phosphite:

$$H_3PO_2 + I_2 + H_2O \rightarrow H_3PO_3 + 2HI.$$

Under certain conditions, the resulting phosphite may be oxidised by iodide to phosphate:

$$H_3PO_3 + I_2 + H_2O \rightarrow H_3PO_4 + 2HI.$$

In a strongly acid medium the first reaction mainly occurs.

A procedure has been developed[138] for the determination of hypophosphite ions in acid chemical nickel-plating solutions based on weighing the nickel–phosphorus coating obtained as a result of the reaction of Ni^{2+} by hypophosphite. Phosphite (up to 50 g litre^{-1}) and reducing agents do not interfere with the determination.

It has been established[139] that in a borate buffer IO_4^- oxidises $H_2PO_2^-$, HPO_3^{2-}, SeO_3^{2-}, and TeO_3^{2-} on heating and in all cases IO_3^- is formed. The excess IO_4^- may be titrated iodometrically in a buffer medium and the content of any of the above substances can thus be found. A procedure has been proposed for the photometric determination[140,141] of $H_2PO_2^-$, based on the decrease of the optical density of the solution at 530 nm due to the reduction of Fe^{3+} to Fe^{2+} by the hypophosphite ion.

Sodium hypophosphite may be determined[142], after the preliminary removal of iron from solution, by oxidising NaH_2PO_2 with an iron(III) salt solution, this being followed by the titration of the Fe^{2+} formed with a cerium(IV) sulphate solution. The kinetics and mechanism of the oxidation of phosphite by cerium(IV) in sulphuric acid solution have been studied[143]. Conditions have been described for the oxidation of hypophosphite ions by various oxidants: nitric acid[144], permanganate[145,146], cerium(IV) salts[147,148], dichromate solution in the presence of silver ions[149], bromide-bromate[150], an iron(III) salt[151], and persulphate (catalysed by bivalent copper in perchloric acid solution)[152].

Organic derivatives of hypophosphorous acid—phosphinous and disubstituted phosphinic acids—are of interest. One or two hydrogen atoms attached to phosphorus in hypophosphorous acid can be substituted by alkyl or aryl groups. When one hydrogen atom is substituted, the resulting compounds are called alkylphosphinous or phosphinous acids RHPOOH. Little is known about the monoesters of these acids, but a number of diesters have been obtained. The acids formed as a result of the substitution of two hydrogen atoms attached to phosphorous in hypophosphorous acid are called dialkylphosphinic (diarylphosphinic) acids or "secondary" phosphinic acids.

The free acids $R_2P(O)(OH)$ and the corresponding esters $R_2P(O)(OR)$ are known.

IX. THE APPLICATIONS OF HYPOPHOSPHITES

From the economic point of view, the applications of hypophosphites for the surface treatment of metals are the most important[153]. This advanced method was proposed in the USA after the Second World War[154] and was subsequently extended, investigated theoretically, and continually improved[155].

Investigations showed[156–159] that metallic plates can be coated chemically by nickel, cobalt, or their alloys with the aid of hypophosphite ions, the resulting thin coating (less than 0.025 mm) being extremely hard, non-porous, and strongly attached to the metal. The thickness of the layer of deposited metal may be regulated. A great advantage of the method is the possibility of treating also non-metallic materials—ceramics, glass, and plastics. In semiconductor engineering it is possible to deposit metallic contacts directly onto ceramics or other materials in the manufacture of transistors[159].

Hypophosphites are also used for the electroplating of various articles[160,161].

The reducing properties of hypophosphites permitted their use in the manufacture of explosives[160]. For example, a mixture of equal amounts of barium hypophosphite and potassium chlorate, the latter subjected to preliminary drying at 100°C, rapidly ignites in open air with a weak explosion. In a closed vessel the mixture detonates. It is readily ignited by an electric spark and is very sensitive to impact and friction.

In view of the use of hypophosphites in pharmaceutical practice at the end of the 19th century, their toxicity has been investigated in very great detail[163-167]. No evidence indicating their toxicity to mammals has been obtained; in the mammallian organism they remain unchanged and are rapidly eliminated.

Hypophosphites have been recently finding increasingly frequent applications in analytical chemistry. Thus a method employing hypophosphite has been developed[168] for the titrimetric determination of iron in the presence of copper ions as the catalyst.

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Reactions of Electronically Excited Radicals and the Quenching of Excited States by Radicals

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The reactions of electronically excited radicals of different types in liquid and solid phases and the electronic structures of the excited radicals and their kinetic characteristics are discussed. A relation is established between the type of excitation and the type of chemical reaction of the excited radicals. The kinetics and mechanisms of the quenching of excited singlet and triplet states by radicals in solid and liquid phases are discussed.
The bibliography includes 160 references.

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I. INTRODUCTION

The interest in the reactions of electronically excited radicals and quenching processes involving radicals has been aroused by the following factors. Firstly, in electronic excitation the atomic skeleton of molecules and radicals changes little; major rearrangements occur only in the electron shell. A consequence of these electronic transformations of the radical is a change in its reactivity. Comparison of the reactivities of radicals in the ground and excited states and determination of a relation between the nature of the excited state and the nature of its chemical reactions is of significant importance for the theory of structure and reactivity. Secondly, excited radicals play a definite role in the degradation of polymers and it is important to know their place and role in the solution of problems concerned with the photoresistant and photolabile polymers. Thirdly, high (nearly unity) quantum yields of reactions are characteristic of radicals and one cannot, therefore, rule out the possibility that radical systems may be promising from the standpoint of utilising solar energy and developing effective methods for its trapping and transformation.

These problems have been studied mainly by empirical procedures, because the reactions of the electronically excited radicals are highly varied and it is extremely difficult to predict theoretically the mode and direction of the reaction and even more so to derive its quantitative characteristics.

This paper surveys the available experimental results obtained for chemical reactions of electronically excited radicals in solid and liquid phases, and an attempt is made to give a general account of such reactions and to establish certain relations. Furthermore, the review deals with the quenching of excited molecules by radicals and with the quenching of excited radicals.

II. PHOTOCHEMICAL REACTIONS OF RADICALS IN THE SOLID PHASE

1. Allyl Radicals

Absorption bands in the region of 230–270 nm, [1-3] 310 nm, [3] 408 nm, [4] and 500 nm [5] have been detected in the absorption spectra of allyl radicals. Quantum-chemical calculations on allyl radicals predict the presence of two absorption bands—in the long-wavelength region with $\lambda_{max} \simeq 450$ nm (a low-intensity electronic transition which is symmetry forbidden), and in the short-wavelength region with $\lambda_{max} \simeq 220$ nm, ($\epsilon \simeq 10^3$–10^4 litre mole^{-1} cm^{-1}). [6-10] Both bands are due to the $\pi \rightarrow \pi^*$ transition. The electronic ground state of the allyl radical is $(b_1)^2 (a_2)$, where b_1 and a_2 are bonding and antibonding orbitals (Fig. 1). The electron transitions from b_1 to a_2 and from a_2 to the antibonding orbital $\bar{b}_1$ give rise to excited states of the radical.

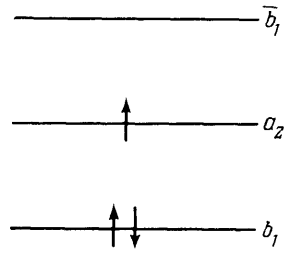


Figure 1. Schematic illustration of the molecular orbitals of the allyl radical.

The photochemical reactions of allyl radicals due to the π–π^* electronic transition can occur by the following mechanisms: (1) intra- or inter-molecular transfer of a hydrogen atom with transformation into an alkyl radical; (2) dissociation of the alkyl radical with elimination of a hydrogen atom.

The photochemical reactions of allyl radicals with γ-irradiated olefins have been investigated[9,10]. The allyl radical CH_2=$CMeCH_2CHMe$ (A), which is transformed under the influence of ultraviolet light (λ = 2537 Å) into the alkyl radical CH_2=$CMeCH_2\dot{C}HMe$ (B) was detected by ESR in 2-methylpent-1-ene (2MP-1) γ-irradiated at 77 K. According to the authors, the photochemical conversion of allyl radicals into alkyl radicals occurs either intramolecularly or intermolecularly. This alternative holds also for all the radicals investigated by Roginskii[11] and

Hamill[12]. To elucidate the possibility, in principle, of an intermolecular transfer of hydrogen atoms, a study was made of the effect of light on the radicals $\dot{C}H_2-CH=CH_2$ formed on γ-irradiation of dilute solutions (frozen glasses) of allyl chloride and allyl bromide in 3-methylpentane (3-MP) [13] and other matrices. On γ-irradiation, allyl radicals are formed as a result of the dissociative capture of slow electrons via the mechanism

$$CH_2=CH-CH_2X + e \rightarrow CH_2=CH-\dot{C}H_2 + X^- \ .$$

Under the influence of light with $\lambda \leqslant 410$ nm, the concentration of allyl radicals falls to zero and 3-MP alkyl radicals appear; the overall concentration of radicals does not change.

The same behaviour has been observed also in other matrices: the decrease in the concentration of allyl radicals under the influence of light is accompanied by a parallel increase of the concentration of alkyl radicals derived from the solvent. These results show that the reactions of allyl radicals proceed without intramolecular isomerisation.

However, two variants of such transformation are possible; the intermolecular abstraction of hydrogen by the excited allyl radical and the dissociation of the latter followed by the interaction with a matrix molecule of the hydrogen atom formed on dissociation. In the former case molecular hydrogen is not formed in the photochemical reaction, while in the latter one H_2 molecule should be evolved for each allyl radical reacting. Gas-chromatographic determination of the yield of molecular hydrogen after the photochemical reaction of allyl radicals showed that the latter do not dissociate, i.e. the allyl → alkyl transformation proceeds via an intermolecular transfer of a hydrogen atom:

$$CH_2=CH-\dot{C}H_2 \xrightarrow{rH,h\nu} CH_2=CH-CH_3 + \dot{r} \ ,$$

where rH is a hydrocarbon.

The photochemical conversion of allyl radicals has also been investigated in olefins (dec-1-ene, oct-2-ene, hept-1-ene, hex-1-ene, and pent-1-ene)[14]. The radiolysis of these olefins results in the formation of alkyl radicals of two types—terminal and central. After being kept for a long time in liquid nitrogen, they are converted into allyl radicals, which are reconverted into alkyl radicals under the influence of light. It is suggested that the transformation occurs as a result of an intramolecular transfer of a hydrogen atom.

To confirm the mechanism involving an intermolecular transfer of a hydrogen atom, a study was made[15] of the effect of light on the allyl type radicals $CH_2=CH-\dot{C}HR$ ($R = C_2H_5$, C_3H_7, or C_4H_9) stabilised in the 3-methylpentane matrix. These radicals were obtained by the radiolysis of solutions of olefins in 3-methylpentane. Under the influence of light, allyl radicals are destroyed and alkyl radicals derived from 3-methylpentane are formed. Molecular hydrogen is not formed in the photolysis of the radicals. Thus in this case too the allyl → alkyl transformation takes place as a result of an intermolecular transfer of a hydrogen atom. Similar results were obtained in another study[16], where the photochemical conversion of radicals in the γ-irradiated isobutene–3-methylpentane system was investigated.

We shall now consider the photochemical reactions of radicals in polymers. Alkyl, allyl, and polyenyl radicals, which may be determined and distinguished on the basis of their ESR spectra, are stabilised in γ-irradiated polyethylene (PE) and polypropylene (PP).[14,16-28] When γ-irradiated polyethylene specimens are kept at room temperature, alkyl radicals are converted into the more stable and long-lived allyl radicals. Under the influence of ultraviolet light ($\lambda = 254$ nm) at 77 K, allyl radicals are reconverted into alkyl radicals[1,17,18], but only up to a limit[1]. The overall concentration of radicals during irradiation remains constant under these conditions.

Fig. 2 presents kinetic curves for the photochemical destruction of allyl radicals and the accumulation of alkyl radicals at 77 K and 25 °C.[1] The limiting ratio of the concentration of alkyl and allyl radicals is independent of the intensity of light and amounts to 43 : 57. The rate of formation of alkyl radicals is proportional to the light intensity and is independent of temperature. The quantum yield of the conversion of the radicals amounts to about 0.1. According to the authors[1], the mechanism of the photochemical reaction involves the transfer of a hydrogen atom via the polymer macromolecule (migration of the valence via the chain):

$$\sim CH_2\dot{C}HCH=CHCH_2CH_2 \sim \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \sim CH_2\dot{C}HCH_2CH=CHCH_2 \sim \ .$$

However, bearing in mind the fairly reliable results obtained in studies on the photochemical reactions of low-molecular-weight allyl radicals, the mechanism involving an intermolecular transfer of a hydrogen atom should probably be adopted in this case too.

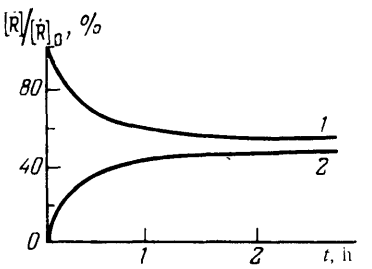


Figure 2. Kinetic curves for the photochemical destruction of allyl radicals and for the accumulation of alkyl radicals: 1) allyl; 2) alkyl.

Since the limiting ratio of the concentrations of alkyl and allyl radicals is independent of the light intensity, one may conclude that the photochemical equilibrium $R^{\cdot}_{all} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} R^{\cdot}_{alk}$ is established, the rate constants for the forward and reverse reactions depending on the light intensity, i.e. the alkyl → allyl transformation is also a photochemical reaction. This result conflicts with data for the kinetics of the photochemical reactions of allyl radicals in polypropylene[29], where the rate of the photochemical transformation of such radicals into alkyl radicals is independent of temperature and varies linearly with light intensity. As in polyethylene, allyl radicals in polypropylene are not fully converted into alkyl radicals, the limiting concentration of the latter obeying the relation

$$[R^{\cdot}_{alk}]_{lim} = \frac{k_1 I [R]_0}{k_1 I + k_2} \ ,$$

where $[R^{\cdot}]_0$ is the initial concentration of radicals and I the light intensity. The constant k_2 is independent of

light intensity, i.e. the reverse reaction $R^{\cdot}_{alk} \rightarrow R^{\cdot}_{all}$ is not photochemical (in conflict with the previous result). However, if it is assumed that the reaction $R^{\cdot}_{alk} \rightarrow R^{\cdot}_{all}$ is a dark process, then it is necessary to assume that the dark reaction proceeds at a high rate, comparable to that of the photochemical reaction $R^{\cdot}_{all} \rightarrow R^{\cdot}_{alk}$ (this follows from the fact that the limiting concentrations of $R^{\cdot}_{all}$ and $R^{\cdot}_{alk}$ are similar). The hypothesis that at the instant of the photochemical transformation $R^{\cdot}_{all} \rightarrow R^{\cdot}_{alk}$ the alkyl radical contains an excess of vibrational energy and for this reason is reconverted into the initial allyl radical is likewise unjustified and cannot account for the attainment of limiting concentrations of $R^{\cdot}_{all}$ and $R^{\cdot}_{alk}$.

Thus the kinetics and mechanism of the photochemical reactions $R^{\cdot}_{all} \rightleftharpoons R^{\cdot}_{alk}$ have been inadequately investigated. Both the forward and reverse reactions probably involve photochemical stages. This is supported by the finding that, at a higher temperature (above 170 K), allyl radicals undergo complete photochemical recombination under the influence of light (by a second-order reaction)[29]. Evidently, the recombination proceeds via photochemically induced relay transfer of valence with participation of alkyl radicals.

2. Polyenyl Radicals

In polyene radicals the energy of the lowest excited state ($\pi-\pi^*$ transition) depends on the number of π electrons in the radical[39]:

$$h\nu = 4\beta \sin \frac{\pi}{2(N+1)} ,$$

where N is the number of π electrons in the radical and β is the resonance integral. Evidently, with increase of the number of π electrons in the radical, the absorption bands should be displaced towards longer wavelengths. Such data for certain conjugated radicals are presented in Table 1.

Table 1. The parameters of the absorption spectra of certain conjugated radicals.

Radical	Matrix	λ^*_{max}, nm	References
$CH_2{=}CH{-}\dot{C}H_2$	Allyl chloride in 3-MP, allyl bromide in cyclohexane	232, 225, 220	3,6,13
Allyl	PP	255	2,30,31
	PE	258	2,30—32
Dienyl	PP	310	2,30—32
	PE	285	2,30—32
Trienyl	PP	368	2,30—32
	PE	323	2,30—32
Tetraenyl	PE	359	2,30—32
Pentaenyl	PE	396	2,30—32
	Cyclohexane	338	33
	Benzene	315	5,34,35
	Toluene	310	34,36—38

*The λ_{max} for the intense absorption bands of radicals only are quoted.

The positions of the electronic levels are relatively insensitive to substituents. For example, the substitution of hydrogen atoms in the allyl radical shifts the maxima of the short-wavelength bands by 10–12 nm.[5] Different substituents (Cl, Br, OH, alkyl, etc.) cause little change in the positions of the electronic levels of the benzyl and cyclohexadienyl radicals[34,37-39].

The photochemical reactions of polyenyl radicals have been investigated in greater detail in polyethylene and polypropylene. Such radicals, having the general formula

$$\sim CH_2{-}\dot{C}H(CH{=}CH)_n CH_2 \sim \text{ (in PE) and } \sim CH_2{-}\dot{C}Me(CH{=}CMeCH_2)_n \sim$$

are formed when polymers are treated with high radiation doses (about 100 Mrad and more), the number of polyenyl radicals with higher values of n increasing as the dose is increased. The ESR spectra of polyenyl radicals consist of a singlet line, which becomes narrower with increase in the length of the conjugation chain.

During the photochemical reaction the conjugation energy of the π-electron system diminishes[29]. With increase in the length of the conjugation chain, the difference between the conjugation energy of the polyenyl radical and the polyene molecular chain increases in absolute magnitude. The difference ΔG, calculated by Hückel's method, is described by the equation

$$\Delta G = 2\pi\left[\sin^{-1}\frac{\pi}{2n} - \cot\frac{\pi}{2(n+1)}\right].$$

It follows from this that there exists a critical value of n in the polyenyl radical for which the energy of the absorbed light quantum is insufficient to compensate the difference between the conjugation energies of the polyenyl radical and the polyene chain. Calculations showed that, for $n > 5$, the photochemical transformation of polyenyl radicals already becomes unfavourable on energy grounds and such radicals should not be converted into alkyl radicals.

In order to determine experimentally the light wavelength at which the transformation of polyenyl radicals begins, γ-irradiated polypropylene specimens were illuminated at 77 K through various light filters. An appreciable change in the ESR spectrum was observed at $\gamma \geqslant 380$ nm. Under the influence of shorter-wavelength light, the ESR spectrum becomes better resolved. The 380 nm light wavelength is apparently limiting; it corresponds to absorption by the polyenyl radical with $n = 3$ ($\lambda_{max} = 385$ nm). With increase of radiation dose, the number of polyenyl radicals having $n > 3$ increases and there is a corresponding decrease of the fraction of radicals having $n \leqslant 3$, which are incapable of being converted into alkyl radicals. For radiation doses in excess of 500 Mrad, photochemical reactions of polyenyl radicals were not observed. This is probably because such doses lead to the formation of appreciable concentrations of polyenyl radicals with $n \geqslant 5$.

3. Alkyl Radicals

The unpaired electron in alkyl radical occupies the p orbital of the carbon atom; its energy level is located between the σ and σ^* levels. Electronically excited states of radicals can be obtained in $\pi-\sigma^*$ and $\sigma-\pi^*$ transitions, where σ and σ^* are the bonding and antibonding orbitals of σ bonds. These transitions are forbidden on symmetry grounds and the corresponding absorption bands are of low intensity. However, they have been observed for certain alkyl radicals. Thus, flash photolysis of $HgMe_2$ [40,41] led

to the observation of the spectrum of the $\dot{C}H_3$ radical. The longest-wavelength absorption band of the radical is located near 216 nm. It is suggested that in the ground and excited states the radical has a planar configuration (sp^2 hybridisation). Weak absorption bands have also been observed in the spectra of other alkyl radicals[42-44]. Thus alkyl radicals absorb light in the range 200–240 nm.

On photoexcitation, alkyl radicals can dissociate, isomerise, or enter into substitution reactions. The photoinduced isomerisation of the t-butyl radical into the isobutyl radical in γ-irradiated isobutyl bromide has been investigated. The ESR spectrum of the t-butyl radical consists of 10 lines with a splitting constant of 25 G and a binomial intensity distribution. On illumination with ultraviolet light at 77 K, the spectrum is converted into one with five lines, i.e. the t-butyl radical isomerises to the isobutyl radical:

$$CH_3-\dot{C}Me_2 \underset{\text{dark}}{\overset{h\nu}{\rightleftharpoons}} \dot{C}H_2-CHMe_2 \quad .$$

The reverse reaction takes place in the dark.

The t-butyl cation is known[45] to have an intense absorption band at 290–295 nm. On the basis of the properties of molecular orbitals, the t-butyl radical presumably also absorbs ultraviolet light at 290 nm, which gives rise to the photoinduced isomerisation.

When isobutene[43] was γ-irradiated, the ESR spectrum of isobutyl radicals CH_2-CHMe_2 was observed, together with a singlet line, which the authors attribute to the 2-methylallyl radical $\dot{C}H_2-CMe=CH_2$. Under the influence of light ($\lambda > 340$ nm), the t-butyl radical is formed, its appearance being associated with the reaction of the electronically excited allyl radical with matrix molecules. On subsequent irradiation with light of shorter wavelengths ($\lambda \leq 340$ nm), the t-butyl radical isomerises to the isobutyl radical.

When the copolymer of tetrafluoroethylene (TFE) and hexafluoropropene was γ-irradiated[46], an ESR spectrum consisting of eight hyperfine structures (HFS) lines with a splitting of 29 G, due to the radical $\sim CF_2-\dot{C}(CF_3)-CF_2\sim$, was recorded. This radical absorbs light with $\lambda_{max} = 265$ nm, being converted into the radical $\sim CF_2-\underset{\displaystyle \dot{C}F_2}{\underset{|}{CF}}-CF_2\sim$, the spectrum of which consists of three lines (a central singlet and two extreme components with a splitting of about 450 G between the latter). It is suggested that the transformation proceeds via the isomerisation of the excited radical according to the mechanism

$$\sim CF_2-\underset{\displaystyle CF_3}{\underset{|}{\dot{C}}}-CF_2\sim \xrightarrow{h\nu} \sim CF_2-\underset{\displaystyle \dot{C}F_2}{\underset{|}{CF}}-CF_2\sim \quad .$$

Similar transformations of radicals have been observed in polypropylene[43] and have also been explained by isomerisation.

A serious difficulty encountered in the studies discussed above is the lack of a reliable and unambiguous interpretation of the ESR spectra of radicals in solid matrices. In γ-irradiated substances allyl as well as alkyl radicals are formed and one cannot rule out the possibility that the reactions of the former obscure the results of the photochemical transformations of the alkyl radicals. Furthermore, the photochemical reactions of alkyl radicals, which are treated as isomerisations, can be interpreted as intermolecular transfer of a hydrogen atom. For this reason, although the occurrence of photochemical isomerisation is in principle possible, additional evidence is required.

As already stated above, in $\pi-\sigma^*$ excitation of alkyl radicals there is a possibility of a photochemical decomposition of the radicals. A number of studies[47,48] have confirmed this hypothesis. Thus, in the photolysis of polypropylene in the presence of nitroxy-radicals the composition and kinetics of the accumulation of gaseous photolysis products was investigated together with the kinetics of the destruction of the nitroxy-radicals[48]. Hydrocarbons (methane, ethane, propane, propene, and isobutene) were detected in the gaseous products. In the presence of nitroxy-radicals the yield of methane increases by approximately a factor of 250, while the yields of the other products depend little on the presence of these radicals. Under these conditions, the photochemical decomposition of nitroxy-radicals is not accompanied by the formation of methyl radicals from them. Evidently the vigorous formation of methane is due to the photochemical decomposition of polypropylene macroradicals. The latter are formed by the mechanism

$$\dot{R}^* + \sim CH_2-CHMe-CH_2\sim \rightarrow RH + \sim CH_2\dot{C}MeCH_2\sim \,,$$

where $\dot{R}^*$ is an electronically excited nitroxy-radical.

The decomposition of central radicals proceeds when macroradicals absorb a light quantum. Thus an electronically excited radical can decompose at any of the three C–C bonds near the localised free valence. However, the decomposition at two of the bonds leads to the formation of terminal macroradicals, while the decomposition at the third bond yields $\dot{C}H_3$. Terminal radicals undergo cage recombination with a high probability, while the light $\dot{C}H_3$ radical diffuses into the bulk, forming methane. The biradical $\sim CH_2-\ddot{C}-CH_2\sim$ formed is converted into the radical $\sim CH_2-\dot{C}H-CH_2\sim$ as a result of reaction with the polymer, the radical $\sim CH_2-\dot{C}Me-CH_2\sim$ being formed simultaneously. The absorption spectra of alkyl radicals in polypropylene are unknown; presumably they absorb in the same region as t-butyl radicals. A similar conclusion concerning the photochemical decomposition of alkyl radicals in polypropylene was reached in another investigation[49].

In the photolysis of isotactic polypropylene[47] in the range $260 < \lambda < 360$ nm the ESR spectrum reveals the presence of the central radical $\sim CHMe-\dot{C}H-CHMe\sim$. Under the influence of light with $\lambda < 270$ nm, this radical is converted into a methyl radical. A similar reaction has also been observed in polyisobutylene.

Methyl radicals are apparently formed in both cases by the decomposition of alkyl radicals in an excited state with occupied antibonding σ^* orbitals. Under these conditions, the dissociation of C–Me bonds in the radical is accompanied by the rupture of other C–C bonds involving the α-carbon atom with decomposition of the macromolecules. However, owing to cage effects, these processes are less important, while the methyl radical leaves the primary cage comparatively readily and avoids recombination.

The effect of light in the range $240 < \lambda < 270$ nm at 77 K on radicals in γ-irradiated 3-methylpentane, 3-ethylpentane, 3-methylheptane, and 4-methylheptane also causes their decomposition and isomerisation[50]:

$$CH_3\dot{C}HCH\,(CH_3)\,CH_2CH_3 \rightarrow C_2H_5 + \text{molecular products},$$
$$CH_3\dot{C}HCH\,(C_2H_5)\,CH_2CH_3 \rightarrow \dot{C}_2H_5 + \text{molecular products},$$
$$CH_3\dot{C}HCH_2CH\,(CH_3)\,CH_2CH_2CH_3 \begin{cases} \rightarrow \dot{C}_2H_5 + \text{molecular products}, \\ \rightarrow \dot{C}H_2CH_2CH_2CH\,(CH_3)\,CH_2CH_2CH_3 \quad . \end{cases}$$

Considerable amounts of ethane were detected among the gaseous products formed in the photolysis of the radicals[50].

4. Peroxy-radicals

Peroxy-radicals absorb light in the band at 240–280 nm [51,52] owing to the transition of an electron from the n orbital of the oxygen atom to the antibonding π^* orbital ($n-\pi^*$ excitation).

When allyl and polyenyl radicals come into contact with oxygen in γ-irradiated polypropylene, peroxy-radicals are formed[53,54]. Their ESR spectra are identical, consisting of an asymmetric line due to the anisotropy of the g-factor. Under the influence of light with $\gamma > 280$ nm, peroxy-radicals are converted into alkyl radicals, but the overall concentration of radicals remains unchanged. The kinetics of the disappearance of peroxy-radicals are described by the first-order equation

$$ROO^{\bullet} + RH \rightarrow ROOH + \dot{R},$$

the rate of the reaction being independent of temperature. Under the influence of short-wavelength light ($\lambda \leq 280$ nm), the hydroperoxide formed dissociates with formation of free radicals[55].

$$ROOH \rightarrow R\dot{O} + \dot{O}H \quad ,$$
$$\dot{O}H + RH \rightarrow \dot{R} + H_2O \quad ,$$
$$R\dot{O} + RH \rightarrow \dot{R} + ROH \quad .$$

As a result, the experimental overall radical concentration increases almost by a factor of three. In the presence of oxygen, when alkyl radicals are continuously converted into peroxy-radicals, all these reactions lead to a chain process with degenerate photochemical branching.

In consequence of the photochemical reactions of peroxy-radicals, the rate of graft polymerisation increases sharply; thus, at a light intensity of 10^{15} quanta $cm^{-2}\ s^{-1}$ ($\lambda < 300$ nm), the rate constant increases by two orders of magnitude compared with that for the dark reaction.

The oxidation of polytetrafluoroethylene (**PTFE**) subjected to preliminary irradiation *in vacuo* at 300 K results in the formation of the central peroxy-radicals $\sim CF_2-\underset{\underset{O-\dot{O}}{|}}{CF}-CF_2\sim$. Under the influence of light ($\lambda < 280$ nm), these radicals are converted into terminal fluoroalkyl radicals[57,58]. The rate of this reaction obeys first-order kinetics, the effective activation energy being about 1 kcal $mole^{-1}$.[57] The following reaction mechanism has been proposed:

$$\sim CF_2-\underset{\underset{O-\dot{O}}{|}}{CF}-CF_2\sim \rightarrow \sim CF_2\dot{C}F_2 + CO + CF_2O + CF_3CF_2\sim \quad .$$

This process is accompanied by the degradation of the polymer chain: the gaseous photolysis products (CO, CF_2O) were identified mass-spectrometrically[59]. In oxygen the terminal **PTFE** allyl radical is oxidised and converted into the terminal peroxy-radical $\sim CF_2-CF_2-\dot{O}O$, the **ESR** spectrum of which at 77 K is completely identical with that of the central peroxy-radical[60-62]. On illumination *in vacuo*, this radical is reconverted into the initial terminal fluoroalkyl radical. The rate of conversion is described by a first-order kinetic equation with an effective activation energy of about 2–3 kcal $mole^{-1}$. The quantum yield of the destruction of peroxy-radicals is close to unity. It is suggested[62] that terminal **PTFE** peroxy-radicals are converted into terminal alkyl radicals in the following way:

$$\sim CF_2CF_2O\dot{O} \xrightarrow{h\nu} 2CF_2O + \sim CF_2\dot{C}F_2 \quad .$$

The detailed mechanism of the photochemical transformations of peroxy-radicals in **PTFE** is unknown. However, presumably the first stage is, as in polypropylene, the conversion of the peroxy-radical in an electronically excited $n-\pi^*$ state into a peroxide via the mechanism

$$\sim \underset{\underset{O\dot{O}}{|}}{CF_2CFCF_2}\sim \xrightarrow{\sim CF_2\sim} \sim \underset{\underset{OOF}{|}}{CF_2CFCF_2}\sim + \sim \dot{C}F\sim \quad .$$

The fluorine-containing peroxide is probably unstable and decomposes photochemically under the influence of light at longer wavelengths than the polypropylene hydroperoxide:

$$\sim \underset{\underset{OOF}{|}}{CF}\sim \xrightarrow{h\nu} \sim \underset{\underset{\dot{O}}{|}}{CF}\sim + \dot{O}F \quad .$$

The subsequent photochemical decomposition of the oxy-radical leads to the formation of a terminal radical:

$$\sim \underset{\underset{\dot{O}}{|}}{CF_2CFCF_2}\sim \rightarrow \sim CF_2C\begin{matrix}O\\ \diagup\\ \diagdown\\ F\end{matrix} + \sim \dot{C}F_2 \quad .$$

Terminal peroxy-radicals probably decompose similarly:

$$\sim CF_2O\dot{O} \xrightarrow{h\nu} \sim CF_2OOF \xrightarrow{h\nu} \sim CF_2\dot{O} \rightarrow CF_2O + \dot{C}F_2 \quad .$$

In the presence of oxygen all these reactions lead to a branched chain process accompanied by the displacement of the free valence by a relay mechanism and the recombination of the radicals. The photo-induced recombination of peroxy-radicals in **PTFE** has not, in fact, been observed. Determination of the fluoride ions formed on hydrolysis of the gaseous photolysis products from peroxy-radicals established that between 50 and 90 fluoride ions are produced for each peroxy-radical which disappears[52]. This result confirms the chain mechanism of the photochemical reactions of peroxy-radicals.

However, the reaction $R\dot{O}_2 + RH \rightarrow RO_2H + R^{\bullet}$ is probably not the only possible pathway whereby excited peroxy-radicals are destroyed. One cannot rule out also the possibility of the decomposition of radicals via the scheme $R\dot{O}_2^{*} \rightarrow R^{\bullet} + O_2$, for example, or via other mechanisms[63]; the situation in this field is not well defined and clear-cut.

5. Radicals Derived from Alcohols, Ethers, and Carbonyl Compounds

In alcohol and ether radicals $R_1R_2\dot{C}OR_3$ (where R_1, R_2, R_3 are hydrogen atoms or alkyl groups) the lone pair electrons of the oxygen atom are involved in conjugation with the unpaired π electron of the carbon atom and the absorption spectra of these radicals are therefore displaced towards longer wavelengths compared with the spectra of alkyl radicals and alcohol and ether molecules. The absorption band maxima of certain alcohol radicals are listed below.

Radical	λ_{max}, nm	References
$CH_2\dot{O}H$	223	64,65
$CH_3\dot{C}HOH$	231	65,66
$C_2H_5\dot{C}HOH$	250	65
$C_3H_7\dot{C}HOH$	244	65
$C_4H_9\dot{C}HOH$	263	65
$C_5H_{11}\dot{C}HOH$	322	65
$(CH_3)_2\dot{C}OH$	250—400	67

The red limit of the absorption of alcohol and ether radicals is near 340 nm. The extinction coefficients are comparatively small, amounting to about 700–900 litre mole^{-1} cm^{-1}.[65,66] The similarity of the optical absorption spectra of these radicals suggests that, when they absorb light, excited states of the same type are produced. On the basis of the results of CNDO calculations on the $\dot{C}H_2OH$ radical[68], the electronic configuration of its ground state can be formulated in terms of the following sequence of molecular orbitals $(1\sigma)^2\ (2\sigma)^2\ (3\sigma)^2\ (4\sigma)^2\ (1\pi)^2\ (5\sigma)^2\ (2\pi)^1$; the unpaired electron is located in the π orbital (80% at the carbon atom and 20% at the oxygen atom). The transfer of the unpaired electron from the 2% orbital to the lowest vacant orbital (6σ) is responsible for the optical absorption of the $\dot{C}H_2OH$ radical in the region with $\lambda < 340$ nm. The $2\pi \rightarrow 6\sigma$ transition is forbidden on symmetry grounds, in agreement with the low extinction coefficient of the $\dot{C}H_2OH$ radical in the range 200–350 nm. Evidently similar electronic transitions occur also in other radicals derived from alcohols and ethers. The principal photochemical reactions of these radicals involve their photochemical dissociation, the mechanism of which is discussed below.

The photochemical reactions of alcohol and ether radicals have been the subject of numerous investigations[69-98]. The primary radicals are formed in alcohols and ethers either on γ-irradiation or on photolysis in the presence of various additives (peroxides, aromatic compounds, stable radicals, etc.). Together with radicals, electrons giving rise to a singlet ESR spectrum ($g \simeq 2.0015$) are stabilised in all alcohols and ethers after γ-irradiation; they give rise to an intense optical absorption in the range 500–600 nm.[65] Under the influence of visible light, ($\lambda > 500$ nm), they are readily destroyed and only alcohol radicals remain.

Light with $\lambda < 320$–350 nm induces the transformations of primary alcohol radicals into secondary radicals. We shall consider them using as an example the photolysis of methanol radicals. The photolysis of the $\dot{C}H_2OH$ radicals has been studied in greatest detail by Shelimov et al.[76] When the full light of the mercury lamp was allowed to act on H_2O_2 and C_6H_6 solutions in methanol at 77 K, the ESR spectra revealed the presence of $H\dot{C}O$ and $\dot{C}H_3$ radicals. In the dark the concentration of $H\dot{C}O$ radicals remained unchanged, while the $\dot{C}H_3$ radicals were destroyed via the reaction $\dot{C}H_3 + CH_3OH \rightarrow CH_4 + \dot{C}H_2OH$. When illumination was switched on again, the ESR spectrum again revealed the presence of $H\dot{C}O$ and $\dot{C}H_3$ radicals. The $H\dot{C}O$ radicals are destroyed under the influence of light with $\lambda > 320$ nm, by the dissociation reaction

$$H\dot{C}O \xrightarrow{h\nu} \dot{H} + CO \quad , \qquad (1)$$

$$\dot{H} + CH_3OH \rightarrow \dot{C}H_2OH + H_2 \quad . \qquad (2)$$

The second reaction results in an increase of the $\dot{C}H_2OH$ concentration.

Mass-spectrometric analysis of the gaseous photolysis products revealed the presence of H_2 (57%), CO (26%), and CH_4 (17%), the composition of the products being independent of the duration of the irradiation. Shelimov et al.[76] proposed two mechanisms for the photolysis of $\dot{C}H_2OH$. The first involves the dissociation of the C–O bond in the radical and presupposes the following sequence of reactions:

$$\dot{C}H_2OH \xrightarrow{h\nu} \ddot{C}H_2 + \dot{O}H \quad , \qquad (3)$$

$$\ddot{C}H_2 + CH_3OH \rightarrow \dot{C}H_3 + \dot{C}H_2OH \quad , \qquad (4)$$

$$\dot{O}H + CH_3OH \rightarrow \dot{C}H_2OH + H_2O \quad . \qquad (5)$$

In the second mechanism it is postulated that the complex of the radical and the molecule absorbs light:

$$(\dot{C}H_2OH + CH_3OH) \xrightarrow{h\nu} \ddot{C}H_2 + H_2O + H\dot{C}O + H_2 \quad , \qquad (6)$$
$$\ddot{C}H_2 + CH_3OH \rightarrow \dot{C}H_3 + \dot{C}H_2OH \quad .$$

Both mechanisms describe a chain process with photochemical branching: a single paramagnetic species destroyed gives rise to three. Both mechanisms presuppose dissociation with formation of carbene ($\ddot{C}H_2$).

The results of other studies[64,79] in which $\dot{C}H_2OH$ radicals were obtained by the radiolysis of frozen methanol are inconsistent with the conclusions that their photolysis has a branched chain mechanism. It was found that illumination with ultraviolet light leads to a decrease of the concentration of $\dot{C}H_2OH$ and the formation of $H\dot{C}O$ radicals, but the total number of radicals remains unchanged.

In the photolysis of $\dot{C}H_2OH$ radicals[68], a decrease of the overall concentration of paramagnetic species was observed, whence the authors concluded that reactions (3) and (6) are not responsible for the formation of $\dot{C}H_3$, because they should have resulted in an increase of the total number of radicals.

According to Chervonenko et al.[94], the main photochemical process in the photolysis of $\dot{C}H_2OH$ is the dissociation of the radicals at the O–H bond:

$$\dot{C}H_2OH \rightarrow H_2CO + \dot{H} \quad . \qquad (7)$$

This mechanism is supported by the maximum yield of H_2 in the photolysis products of the $\dot{C}H_2OH$ radical relative to other products, and also the finding that large amounts of $\dot{C}_2H_5$ radicals are formed by addition in the photolysis of $\dot{C}H_2OH$ in the presence of ethylene as the acceptor of hydrogen atoms, while the rate of destruction of $\dot{C}H_2OH$ increases markedly owing to the suppression of the competing reaction (2).

The dissociation of the O–H bond in the $\dot{C}H_2OH$ radical is favourable on energetic grounds: its energy is less than 1.5 eV. CNDO calculations on the radical[68] have also shown that, when the π electron is excited to the lowest vacant σ orbital, the O–H bond order diminishes, i.e. the bond is weakened, since this σ orbital is antibonding in relation to the O–H bond.

Thus the dissociation of the O–H bond on π–σ^* excitation of the $\dot{C}H_2OH$ radical constitutes one of the principal mechanisms involved in the transformations of the radical. Other reactions of the radical, leading to the formation of $\dot{C}H_3$, are much less definite and unambiguous.

Two mechanisms have now been proposed for the formation of the methyl radical on excitation of $\dot{C}H_2OH$. The first, involving the dissociation of the radical at the C–O bond, was discussed above and the second proposed by Chervonenko[68], presupposes decomposition according to the following scheme:

$$H_2\dot{C}OH \ldots \underset{\displaystyle CH_3}{\overset{\displaystyle |}{OH}} \xrightarrow{h\nu} H_2CO + H_2O + \dot{C}H_3 \quad . \qquad (8)$$

In this mechanism an important role is attributed to the hydrogen bond between the radical and a neighbouring alcohol molecule.

The first pathway should lead to the "multiplication" of $\dot{C}H_3$ radicals, since the photolysis of $\dot{C}H_2OH$ is a chain process with degenerate photochemical branching. The fact that such "multiplication" is frequently not observed in the photolysis of $\dot{C}H_2OH$ at first sight conflicts with the first mechanism. However, one should bear in mind that according to the photolytic mechanism

$$\dot{C}H_2OH \xrightarrow{h\nu} (\ddot{C}H_2, \dot{O}H) \rightarrow (\dot{C}H_3, \dot{O}H, \dot{C}H_2OH)$$

three radicals are formed in a single "cage" and for this reason the probability of the recombination of any radical pair is high, so that the probability of degenerate branching (i.e. the radical "multiplication" factor) is low. If it is less than the probability of the destruction of radicals as a result of recombination in the bulk phase, a decrease of radical concentration is observed on photolysis. Therefore, the absence of the "multiplication" of $\dot{C}H_3$ radicals on photolysis is not by itself an argument against the first mechanism.

The energy of the C–O bond in the ground state of the $\dot{C}H_2OH$ radical is 3.6 eV, However, CNDO calculation has shown[68] that, on $\pi-\sigma^*$ excitation of the radical, the bond is strengthened and its order increases from 0.40 (in the ground state) to 0.80. The C–O bond is also strengthened on deprotonation of the $\dot{C}H_2OH$ radical, i.e. when it is converted into $\dot{C}H_2O^-$ (in alkaline media). In conformity with this, the yield of $\dot{C}H_3$ radicals in the photolysis of $\dot{C}H_2OH$ in alkaline media decreases. These observations are inconsistent with the first mechanism.

The second mechanism agrees with the facts quoted above and formally provides a quite satisfactory explanation of the composition of the photolysis products. We believe that there is a difficulty in the operation of this mechanism in that the excitation region and the region where the excitation energy is utilised are very remote in the $CH_2OH...\underset{|}{\underset{CH_3}{O}}H$ molecular system. In other words, it is difficult to imagine how the excitation of the CH_2–O fragment in the radical leads to the dissociation of the C–O bond in the alcohol molecule. It is unlikely that the entire process takes place in a single fundamental step. Admittedly it is possible that the excitation energy is transferred from the $\dot{C}H_2OH$ radical to the triplet level of the alcohol molecule with its subsequent dissociation, but the probability of such a spin-forbidden process is hard to estimate. Thus the problem of the mechanism of the formation of $\dot{C}H_3$ radicals on photolysis of $\dot{C}H_2OH$ still remains open.

The photolysis of $CH_3\dot{C}HOH$ radicals in ethanol leads to the formation of $\dot{C}_2H_5$ [79,80,82,88] and $Me\dot{C}O$ radicals (they give rise to an intense asymmetric singlet in the ESR spectrum). H_2, CH_4, CO, C_2H_6, H_2O, and acetaldehyde have been detected in the photolysis products[80,94]. The main pathway in the photochemical transformation of $Me\dot{C}HOH$ radicals involves decomposition at the O–H bond with formation of acetaldehyde and a hydrogen atom:

$$CH_3\dot{C}HOH \rightarrow CH_3CHO + \dot{H} \quad . \qquad (9)$$

Hydrogen is the main product of the photolysis of alcohol radicals and is formed mainly via reaction (9). This conclusion is confirmed by the photolysis of $Me\dot{C}HOH$ at various pH values: in alkaline media, where the radical exists in the form of the radical-anion $CH_3\dot{C}HO^-$, the yield of hydrogen is much lower than in acid media. The quantum yield of reaction (9) has been estimated as (0.3 ± 0.2) from the initial rates of accumulation of H_2.[68]

The rate of formation of H_2 in ethanol is much higher than the rate of destruction of $Me\dot{C}HOH$, i.e. the photolysis of the radicals is a chain process in which photochemical chain propagation stages [reaction (9)] and dark stages, involving the regeneration of the initial radical, alternate:

$$\dot{H} + CH_3CH_2OH \rightarrow H_2 + CH_3\dot{C}HOH \quad . \qquad (10)$$

Chain termination proceeds mainly via radical recombination.

Reaction (9) results in the formation of acetaldehyde, the photodissociation of which leads to the appearance of acyl radicals $Me\dot{C}O$. Apart from $\dot{C}_2H_5$ and $Me\dot{C}O$, methyl radicals have also been detected in the photolysis of alcohol radicals. They are formed on photodissociation of the $Me\dot{C}O$ radical and not via the dissociation of the C–O bond in the alcohol radical via the mechanism

$$CH_3\dot{C}HOH \rightarrow \dot{C}H_3 + \ddot{C}HOH \quad , \qquad (11)$$

which has been discussed in a number of investigations[73,82]. Indeed, methane was detected in the reaction products only after the decomposition of $Me\dot{C}O$ radicals by visible light[68].

$\dot{C}_2H_5$ radicals may be formed in the photolysis of alcohol radicals via two mechanisms [reactions (3), (4), and (8)], which were discussed above. The quantum yield in the formation of $\dot{C}_2H_5$ is 0.03 ± 0.02, i.e. is an order of magnitude lower than the quantum yield of the main reaction [reaction (9)].

The photolysis of alcohol radicals in deuterated ethanols[78] C_2H_5OD, CH_3CD_2OH, CD_3CH_2OH, and CD_3CD_2OH results in the formation of the radicals $\dot{C}_2H_5$, $CH_3\dot{C}D_2$, $CD_3\dot{C}H_2$, and $CD_3\dot{C}D_2$ respectively. However, these results do not allow an unambiguous choice of the mechanism of their formation.

The photolysis of the primary radicals $(CH_3)_2\dot{C}OH$ in isopropyl alcohol results in the formation of $(CH_3)_2\dot{C}H$ [67,79,99] and $R\dot{C}O$ radicals do not appear. The main photolysis products are H_2, C_3H_8, and acetone[68,98]. The primary radicals are photolysed by the same mechanism as in the case of other alcohols. In contrast to straight-chain alcohols, acetone is formed in this case and not an aldehyde. Since aldehydes are precursors of $R\dot{C}O$ radicals, their absence in the photolysis of $(CH_3)_2\dot{C}OH$ in isopropyl alcohol is quite reasonable.

On prolonged photolysis of $(CH_3)_2(\dot{C}H_2)COH$ radicals in t-butyl alcohol[68,73,84,98], new radicals are not formed and gaseous products have also not been observed. The stability of these radicals towards ultraviolet light (λ = 310 nm) can be accounted for by the absence of optical absorption by these paramagnetic species in the region $\lambda \geqslant 300$ nm.[100]

The photolysis of the primary radicals $Me\dot{C}HOCH_2CH_3$ derived from ethyl ether leads to the formation of the $\dot{C}_2H_5$ and $Me\dot{C}O$ radicals[68,82]. The main photolysis product is ethane, and molecular hydrogen is not formed. This implies that the principal mechanism of the photolysis of these radicals is their decomposition at the C–O bond in the β-position:

$$CH_3\dot{C}HOC_2H_5 \rightarrow CH_3CHO + \dot{C}_2H_5 \quad . \qquad (12)$$

Thus both the nature of the excited state of the radical and the mechanism of its decomposition remain the same as for alcohol radicals. Even the quantum yields of reactions (12) and (9) are identical, amounting to 0.3 ± 0.2.[68] As in the case of ethanol, the dissociation of acetaldehyde leads to the formation of the acyl radicals $Me\dot{C}O$, from which $\dot{C}H_3$ radicals are formed. Methane appears (as in ethanol) after $Me\dot{C}O$ radicals are exposed to visible light.

The rates of change of the ESR spectra when $Me\dot{C}HOC_2H_5$ radicals are acted upon by light in alkaline and acid solutions of the ether are the same as in the ether itself. This finding shows that the $Me\dot{C}HOC_2H_5$ radical is not involved in protonation and deprotonation reactions (in contrast to alcohol radicals, see above).

When the $C_2H_5\dot{C}HOC_3H_7$ radicals derived from propyl ether were acted upon by light, the n-$\dot{C}_3H_7$ and $C_2H_5\dot{C}O$ radicals were detected[68]; under the influence of visible light, the latter decompose with formation of $\dot{C}_2H_5$ radicals. H_2, C_2H_6, and C_3H_8 were detected in the gaseous photolysis products. Evidently in this case the photolysis of the radicals also proceeds via mechanisms involving the dissociation of the bond in the β-position relative to the atom with the unpaired electron.

On photolysis of the primary $Me_2\dot{C}OCHMe_2$ radicals in isopropyl ether, $Me_2\dot{C}H$ radicals are formed[68]. When they are kept in the dark at 77 K, the initial radicals are regenerated. As in other ethers, H_2 is not formed. In contrast to straight-chain ethers, in this case acetone is produced, as in isopropyl alcohol, and not an aldehyde. For this reason RCO radicals are absent in the photolysis of $Me_2\dot{C}OCHMe_2$.

When straight-chain alcohols and ethers are photolysed together with $R\dot{C}H_2$ radicals, a single asymmetric line also appears in the ESR spectrum, its intensity decreasing under the influence of light with $\lambda > 500$ nm; alkyl radicals $R\dot{C}H_2$ appear under these conditions.

The interpretation of the singlet is extremely contradictory. Many investigators[75,79,80,86,88,93] attribute it to alkoxy-radicals RO, which are formed either during the isomerisation of RĊHOH radicals or when a hydroxyl hydrogen atom is abstracted from ROH. Both processes are unlikely. It is more reasonable to assume[68,82,92,94] that the singlet is due to acyl radicals RĊO, which are derived from the formyl radical HĊO.

There are many common features in the photochemical behaviour of the species responsible for the singlet and of the HĊO radical. Like the HĊO radical, acyl radicals absorb light in the range 400–650 nm. The values of λ_{max} in the absorption spectra of certain acyl radicals in γ-irradiated acyl chlorides and methyltetrahydrofuran at 77 K are listed below[90]:

Radical	λ_{max}, nm
$CH_3\dot{C}O$	340, 500, 540
$C_2H_5\dot{C}O$	330, 480, 540
$PhCH_2\dot{C}O$	320, 510, 550
$Ph\dot{C}O$	320, 450
$Ph{-}CH{=}CH\dot{C}O$	400, 500, 550

The angle between the bonds in the HĊO radical is about 120°; in its ground state the radical is appreciably bent and the unpaired electron is localised in the sp^2 hybrid orbital of the carbon atom[101,102]; the g-factor of the radical is 2.0008. Acyl radicals have been obtained as a result of the dissociative addition of electrons to the molecules of acid chlorides on γ-irradiation[90]:

$$RCXO + e \rightarrow R\dot{C}O + X^- ,$$

their g-factor being 2.0010 and $a_{\alpha-H} = 5.1$ G. Acyl radicals are σ-electron radicals; as in HĊO, the unpaired electron is localised in the sp^2 hybrid orbital of the carbon atom; the unpaired electron density at the atom amounts to 52%.[103] The weak absorption by acyl radicals RĊO in the range 400–650 nm is probably due to a transition from the state in which the CCO angle is close to 120° to one where it is 180°. In the case of $CH_3\dot{C}O$ this corresponds to the excitation of the electron from the singly occupied σ orbital to the lowest vacant π orbital.[68]

Like HĊO radicals, on σ–π^* excitation acyl radicals dissociation with formation of carbon monoxide and R radicals. The energy of the dissociation

$$R\dot{C}O \rightarrow \dot{R} + CO \qquad (13)$$

is about 0.5 eV.[104] Carbon monoxide adds reversibly in the dark to the primary alcohol and ether radicals with formation of the corresponding acyl radicals $R\dot{C}HOH$ and $R\dot{C}HOR$.[68,92] Under the influence of visible light, the latter again decompose with regeneration of the initial radical.

$\dot{C}H_2COMe$ radicals are stabilised at 77 K in γ-irradiated acetone[105]. The action of light with $\lambda < 340$ nm lowers their concentration and leads to the appearance of lines due to the methyl radical[105–107]. For low conversions, the overall radical concentration hardly changes. A single ESR line, the intensity of which increased linearly with time, was observed simultaneously with the methyl radical.

The following mechanism has been proposed for the photochemical reactions[107]:

$$\dot{C}H_2COCH_3 \xrightarrow{h\nu} CH_2{=}C{=}O + \dot{C}H_3 , \qquad (14)$$

$$\dot{C}H_3 + CH_3COCH_3 \rightarrow CH_4 + \dot{C}H_2COCH_3 . \qquad (15)$$

The single line, which is insensitive to either visible or ultraviolet light, was not identified.

The study of the dependence of the rate of accumulation of methyl radicals on the wavelength of the exciting light yielded a spectrum representing the effect of the light on the acetonyl radical[106] which is virtually identical with the absorption spectrum of acetone (280–340 nm). However, it is difficult to conclude that either the acetonyl radical itself absorbs light in this region or there is energy transfer from the excited acetone molecule to the radical; there is a possibility under these conditions of excitation to a higher electronic state of the radical which then dissociates. These hypotheses require proof.

The photochemical reactions of the radicals obtained from ethyl methyl ketone and the isopropyl methyl ketone are similar, i.e., as in the case of acetone, photolysis ($\lambda \leq 340$ nm) leads to the formation of both methyl and alkyl radicals[108]:

$$CH_3\dot{C}HCOCH_3 \xrightarrow{h\nu} CH_2{=}C{=}O + \dot{C}_2H_5 , \qquad (14a)$$

$$Me_2\dot{C}COCH_3 \xrightarrow{h\nu} Me_2\dot{C}H + CH_2{=}C{=}O . \qquad (14b)$$

However, whereas one can assume that $\dot{C}H_3$ is formed in reaction (14) via the dissociation of the C–C bond in the β-position, this cannot be postulated for reactions (14a) and (14b). Their mechanism remains obscure and is hardly likely to involve a single fundamental step.

Together with alkyl radicals, a singlet appears in the ESR spectra on photolysis of ethyl methyl ketone and isopropyl methyl ketone; the authors[108] correctly attributed it to acyl radicals RĊO, which decompose under the influence of visible light ($\lambda > 400$ nm) with formation of alkyl radicals and carbon monoxide (as in the photolysis of alcohols). H_2, hydrocarbons, and CO were detected among the gaseous photolysis products.

The radicals derived from monocarboxylic acids and anhydrides absorb light in the region $\lambda \leq 350$ nm. The absorption band maxima and the extinction coefficients are listed in Table 2.[109]

The radicals $\dot{C}$–COOH absorb at longer wavelengths than the corresponding acids. This effect is a consequence of the interaction of the unpaired electron at the α-carbon atom with the electrons of the adjacent COOH

group. The $\dot{C}H_2Me_2CCOOH$ radicals, in which the unpaired electron is located at the β-carbon atom, do not absorb light with $\lambda > 300$ nm.

Table 2. Parameters of the absorption spectra of radicals derived from monocarboxylic acids.

Acid	pH	Radical	λ_{max}, nm	ϵ, litre mole^{-1} cm^{-1}
Acetic	3	$\dot{C}H_2COOH$	320	650
	10	$\dot{C}H_2COO^-$	350	800
Propionic	3	$CH_3\dot{C}HCOOH$	300	700
	10	$CH_3\dot{C}HCOO^-$	335	900
Butyric	3	$CH_3CH_2\dot{C}HCOOH$	280	—
	9	$CH_3CH_2\dot{C}HCOO^-$	335	900
Trimethylacetic	3	$\dot{C}H_2Me_2CCOOH$	240	—
	9	$\dot{C}H_2Me_2CCOO^-$	240	1800

It follows from CNDO calculations on the electronic state of the $\dot{C}H_2COOH$ radical[68,110] that its excited state is obtained when an electron passes from a doubly occupied σ orbital to a singly occupied π orbital. The σ bonds in the radicals of acids and anhydrides are then weakened and readily dissociate. Indeed, as will be shown subsequently, such dissociation constitutes the principal mechanism of the photochemical reactions of the radicals.

When light at wavelengths in the range $300 < \lambda < 400$ nm was allowed to act on the $\dot{C}H_2COOH$ radical in acetic acid, the radical was destroyed with the simultaneous increase of the $\dot{C}H_3$ concentration[109-111] and the appearance in the ESR spectrum of an asymmetric singlet. The paramagnetic species responsible for this line are destroyed under the influence of light with $\lambda \geqslant 500$ nm, being converted quantitatively into $\dot{C}H_2COOH$ radicals; there is no doubt that these species are the acyl radicals $\dot{C}H_2(CO)COOH$. The principal gaseous products of the photolysis of $\dot{C}H_2COOH$ radicals are CH_4 and CO_2,[110] which are obtained in equal amounts.

The main photochemical process in the photolysis of the $\dot{C}H_2COOH$ radical is, according to Chervonenko and Roginskii[110], the dissociation of the radicals at the C–OH bond:

$$\dot{C}H_2C(=O)OH \rightarrow CH_2=C=O + \dot{O}H \ . \qquad (16)$$

The dissociation of the C–OH bond in the $\dot{C}H_2COOH$ radical is more favourable on energetic grounds; its energy amounts to about 2.5 eV. CNDO calculation on the radical[68] also showed that the C–OH bond order does not decrease on $\sigma-\pi^*$ excitation.

Presumably the methyl radical is formed by the reactions

$$\dot{C}H_2COOH \rightarrow \dot{C}H_3 + \dot{C}OOH \ , \qquad (17)$$

$$\dot{C}H_3 + CH_3COOH \rightarrow \dot{C}H_2 + \dot{C}H_2COOH \ . \qquad (18)$$

However, the most probably mechanism is apparently photolysis of keten. Calculation by the CNDO method has also shown that the C–C bond in the radical is strengthened on $\sigma-\pi^*$ excitation and its order increases from 0.45 (in the ground state) to 0.63, i.e. reaction (17) is unlikely.

Another mechanism for the formation of the methyl radical has been proposed in other investigations[65,68], presupposing the decomposition of the radical in accordance with the scheme

$$\dot{C}H_2C(O\cdots HO)(OH)(O=)CCH_3 \rightarrow CH_2=C(OH)_2 + CH_3C\dot{O}_2 \ , \qquad (19)$$

$$CH_2=C(OH)_2 \rightarrow CH_2=C=O + H_2O \ , \qquad (20)$$

$$CH_3C\dot{O}_2 \rightarrow \dot{C}H_3 + CO_2 \ . \qquad (21)$$

An important role is attributed in this mechanism to the hydrogen bond between the radical and the adjoining acid molecule. This mechanism resembles that postulated for the photolysis of alcohol radicals; the difficulties in its operation were discussed above.

In propionic acid $Me\dot{C}HCOOH$ radicals are destroyed under the influence of light at wavelengths in the range $300 \leqslant \lambda < 400$ nm and $\dot{C}_2H_5$ radicals accumulate[110]. A singlet is not observed in the ESR spectrum. Photolysis terminates after the complete conversion of $Me\dot{C}HCOOH$ radicals into C_2H_5; the principal gaseous photolysis products are ethane and CO_2.

The formation of the $\dot{C}_2H_5$ radical and the accumulation of C_2H_6 and CO_2 in the gaseous products are consistent with the mechanisms discussed in connection with the photolysis of $CH_2\dot{C}OOH$ radicals derived from acetic acid. The absence of $Me\dot{C}H(C=O)COOH$ radicals can probably be accounted for by the rigidity of the propionic acid matrix in which CO is hardly formed owing to the high probability of the reverse reaction between the keten dissociation products. The photochemical behaviour of the $C_2H_5\dot{C}HCOOH$ radicals derived from butyric acid[110] is analogous to the behaviour of $\dot{C}H_2COOH$ radicals in acetic acid. Under the influence of light at wavelengths in the range $300 < \lambda < 400$ nm, the concentration of primary radicals fell and $\dot{C}_2H_5$ and n-$\dot{C}_3H_7$ radicals appeared. As in other acids, C_3H_8 and CO_2 were detected in the photolysis products. The mechanisms of the formation of n-$\dot{C}_3H_7$ and $C_2H_5CH(\dot{C}O)COOH$ radicals and of the photolysis products are analogous to those discussed previously. The primary radicals $C_2H_5CH_2\dot{C}HCOOH$ derived from valeric acid undergo similar reactions[110].

The photochemical behaviour of the protonated radical-anions $(RCH_2\dot{C}OO)^{2-}$, obtained on γ-irradiation of monocarboxylic acids at 77 K, is somewhat unusual[112]. Under the influence of light with $\lambda \geqslant 380$ nm, these radicals disappear irreversibly without the formation of other paramagnetic species. The mechanism of the photolysis probably consists in the protonation of the radical-anions and liberation of electrons with subsequent capture of the electrons by positive ions:

$$(RCH_2\dot{C}OO)^{2-} H^+ \rightarrow RCH_2COOH + e \ , \qquad (22)$$

$$e + (RCH_2\dot{C}OOH)^+ \rightarrow RCH_2COOH \ . \qquad (23)$$

Other radicals are not formed in the photolysis, so that $(RCH_2\dot{C}OO)^{2-}H^+$ radicals do not dissociate and the recombination of $(R\dot{C}OO)^+$ and e explains the decrease of the concentration of paramagnetic species on photolysis.

After γ-irradiation at 77 K the radicals $R\dot{C}H{-}C(=O)O{-}C(=O){-}CH_2R$ are stabilised in monocarboxylic acid anhydrides[113]. These radicals dissociate under the influence of light at wavelengths in the range $300 < \lambda < 400$ nm similarly to radicals

derived from acids, i.e. with dissociation of the bond in the β-position:

$$R\dot{C}HCOCCH_2R \xrightarrow{h\nu} RCH{=}C{=}O + RCH_2C\dot{O}_2 \quad , \tag{24}$$

$$RCH_2C\dot{O}_2 \rightarrow R\dot{C}H_2 + CO_2 \quad , \tag{25}$$

$$R\dot{C}H_2 + (RCH_2CO)_2O \rightarrow RCH_3 + R\dot{C}HCOCCH_2R \quad . \tag{26}$$

The quantum yield of reaction (24) in acetic anhydride is 0.8 ± 0.2.[113] Hydrocarbons, CO_2, and CO were detected in the gaseous photolysis products. The formation of hydrocarbons and CO_2 can be explained by the proposed mechanism and the detection of appreciable amounts of CO in the products is evidence for the formation of ketens, which effectively decompose under the influence of light with $\lambda \geq 300$ nm, forming CO.

6. Amine and Amide Radicals

When amines are γ-irradiated, radicals are formed by the abstraction of a hydrogen atom from the carbon atom in the α-position with respect to the heteroatom[114,115]. The hyperfine structure in the spectra of such radicals in an adamantane matrix is satisfactorily resolved[116].

As in alcohol radicals, in amine radicals the unpaired electron interacts with the lone pair of electrons at the nitrogen atom, which leads to a bathochromic shift of the absorption spectra of the radicals relative to the initial molecules[117]. The absorption spectra of amine radicals contain an intense broad band, the long-wavelength limit of which is at $\lambda \leq 400$ nm. The structure of the radicals obtained on γ-irradiation of amines and on subsequent illumination with ultraviolet light is indicated below together with the λ_{max} for the absorption bands of the radicals.

Amine	Radical after γ-irradiation	λ_{max}, nm	Radicals formed on illumination with ultra-violet light
CH_3NH_2	$\dot{C}H_2NH_2$	230	$CH_2\dot{N}$
Me_2NH	$\dot{C}H_2NHCH_3$	—	$Me_2\dot{N}$
Me_3N	$\dot{C}H_2NMe_2$	260	$Me_2\dot{N}$, $\dot{C}H_3$
$C_2H_5NH_2$	$CH_3\dot{C}HNH_2$	240	$\dot{C}_2H_5$, $CH_3CH{=}\dot{N}$
$(C_2H_5)_3N$	$CH_3\dot{C}HN(C_2H_5)_2$	250	$\dot{C}_2H_5$
$(C_2H_5)_2NH$	$CH_3\dot{C}HNHC_2H_5$	—	$\dot{C}_2H_5$

The most probable photochemical process on excitation of amine radicals is (as in alcohol radicals) their photodissociation with formation of various products.

The evidence for the mechanisms of the photochemical reactions of amine radicals is weak. Certain hypotheses have been put forward in a number of studies[114,115,118] concerning the photochemical dissociation of the N–R bonds in $\diagup\dot{C}$–NH–R radicals (where R = H, Me, C_2H_5, etc.). The dissociation of the N–R bond is probably the main photochemical reaction of amine radicals. In addition there is also the possibility of the dissociation of the C–N bond in the radical. However, the probability of this reaction is much lower than that of the dissociation of the N–R bond in the β-position (by analogy with radicals derived from alcohols, ethers, and other carbonyl compounds discussed in the previous section).

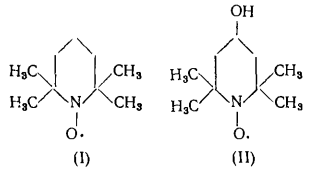
As in alcohols and ethers, the active radical species ($\dot{C}H_3$, $\dot{C}_2H_5$, $Me_2\dot{N}$, $H^{\cdot}$) formed in amines under the influence of light abstract hydrogen in the dark from the matrix molecules with regeneration of the initial photochemically active radicals.

When amine salts, in which there is no lone electron pair (a proton is attached to it), are γ-irradiated, $\diagup\dot{C}\overset{+}{N}H\diagdown^{R_1}_{R_2}$ radicals are formed following the abstraction of a hydrogen atom from the α-carbon atom[119]. Under the influence of light ($\lambda > 260$ nm), there is no photodissociation of radicals, the form of the ESR spectra of the radicals remains unchanged, and gas evolution is not observed. This is associated with the fact that the absorption by radicals of amine salts in which there is no $n-\pi$ conjugation, is displaced towards shorter wavelengths ($\lambda < 260$ nm), compared with the absorption by the corresponding radicals with a lone electron pair. Radicals of the type $\diagup\dot{C}\overset{+}{N}HR_1R_2$ therefore behave similarly to alkyl radicals.

III. PHOTOCHEMICAL REACTIONS OF RADICALS IN THE LIQUID PHASE

1. Nitroxy-Radicals

Nitroxy-radicals of the type



(I) (II)

do not react in the ground state with hydrocarbons up to a temperature of about 100°C, but, on being excited with radiation corresponding to the $\pi-\pi^*$ absorption band of the N–O group ($\lambda_{max} = 240$ nm, $\epsilon = 1500$), the radicals are destroyed even at a comparatively low temperature (about 10°C).[121,122] The main photolysis products are hydroxylamine and ether—the product of the recombination of nitroxy- and alkyl radicals[123]. The yields of each of these radicals are the same, amounting to about 50%.

The kinetic mechanism of the destruction of the radical can be represented as follows:

$$\dot{R} \xrightarrow{h\nu} \dot{R}^* \text{ (excitation of the radical)},$$
$$\dot{R}^* \xrightarrow{f} \dot{R} \text{ (radiative deactivation)},$$
$$\dot{R}^* \xrightarrow{d} \dot{R} \text{ (radiationless deactivation)},$$
$$\dot{R}^* + rH \xrightarrow{r} RH + \dot{r} \text{ (destruction of the radical)},$$
$$\dot{R} + \dot{r} \rightarrow Rr \quad .$$

The rate of destruction of radicals for $\bar{\epsilon}[R]l \ll 1$ is defined by the equation

$$-\frac{d[\dot{R}]}{dt} = \frac{2r[rH]\,n_0\bar{\epsilon}l}{f+d+r[rH]}[\dot{R}]$$

or

$$\lg\frac{[\dot{R}]_0}{[\dot{R}]} = \frac{0{,}87r[rH]\,n_0\epsilon l}{f+d+r[rH]} \quad ,$$

where n_0 is the number of incident photochemically active quanta and $\bar{\epsilon}$ is the effective extinction coefficient.

The quantum yields of the reaction $\gamma = r[rH]/\{f + d + r[rH]\}$ were found from the equation of Bogatyreva et al.[122], and the activation energies for the abstraction of a hydrogen atom from solvents by the electronically excited

radicals (I) were determined from the temperature variation of $(f + d)/r$ (provided that $f + d$ depends only slightly on temperature). These results are listed in Table 3.

The high quantum yields and the low activation energies [the activation energy for the reaction of the radical (I) is 34 kcal mole^{-1} [124]] show that in an electronically excited state the radical (I) is highly reactive.

Table 3. The quantum yields and activation energies E for reactions involving the abstraction of a hydrogen atom by the electronically excited radical (I).[122]

Solvent	10° C	18° C	25° C	E, kcal mole^{-1}
Heptane	0.32	0.37	0.42	2.3
Toluene	0.51	0.61	0.68	2.5
Cyclohexane	0.30	0.37	0.42	3.0
Water	0.16	0.31	0.42	9.1

The quenching of the electronically excited state of the radical (I) by oxygen in heptane and water and by nitric oxide in heptane[122] obeys the Stern–Volmer equation, from which the values of $k_q\tau$ were found, k_q being the quenching rate constant and τ the lifetime of the radical. The constant k_q was assumed equal to the rate constant for the diffusional encounters of radicals and was determined from the broadening of the ESR spectra of the radicals in the presence of oxygen and nitric oxide[125]. The observed values of k_q and the calculated τ are listed in Table 4.

Table 4. The values of k_q and τ for the radical (I).

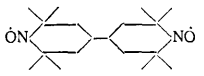
System	k_q, litre mole^{-1} s^{-1}	τ, s
Heptane + O_2	$1.6\cdot10^{10}$	$5.7\cdot10^{-8}$
Water + O_2	$8.7\cdot10^{10}$	$6.3\cdot10^{-8}$
Heptane + NO	—	$4.6\cdot10^{-8}$

The spectrum of the nitroxy-radical (I) contains two absorption bands corresponding to $\pi-\pi^*$ and $n-\pi^*$ excitations[126]. According to molecular spectroscopic data, the lowest excited state is the most stable and long-lived and the radiationless transitions from the highest electronic and vibrational levels to the lowest excited level take place at a high rate[127]. The radical (I) has the $n-\pi^*$ low-excited state. The dipole moment of the radical (I) in the excited state has been determined from the shifts of the $n-\pi^*$ absorption band in different solvents[122]. It was found that, on excitation of the radical, its dipole moment decreases from 3.14 D in the ground state[128] to 1.0 ± 0.8 D in the excited state. On $n-\pi^*$ excitation, there is probably a partial charge transfer from the oxygen atom (from the lone electron pair) to the delocalised π^* orbital. As a result, there is a deficiency of electrons at the reaction centre, which must be the cause of the high reactivity of the radical (I) in the electronically excited state.

Furthermore, this state must be comparatively long-lived, because an activation energy is required for the reaction of the excited radical. These considerations are consistent with experimental results. Evidently, reactions involving the abstraction of a hydrogen atom by the excited nitroxy-radicals proceed in the $n-\pi^*$ state.

The photolysis of the radicals (I) in the solid state takes place in accordance with the mechanism discussed for the photolysis of these radicals in the liquid phase[49].

The photochemical behaviour of the biradical



(III)

is of interest, because it contains two reaction centres whose unpaired electrons are involved in exchange reactions on intramolecular collisions. It was found that the quantum yield of the reaction of the biradical is the same as the quantum yield of the reactions of monoradicals[121], i.e. the quenching due to intramolecular collisions between the radical centres is insignificant. This implies that the period τ_0 between these collisions is greater than the lifetime of the excited radical τ, i.e. $\tau_0 > 10^{-8}$ s.

It was found in the photolysis of the radical (I) in a dense gas (ethane under a pressure of 50 atm) that the lifetime of the electronically excited radical is greater than in the liquid phase. This fact is probably due to the decreased rate of deactivation $(f + d)$ of the radical in the gas phase compared with the liquid phase.

2. Diphenylpicrylhydrazyl (DPPH)

The electronic spectrum of DPPH contains two bands corresponding to the $\pi-\pi^*$ and $n-\pi^*$ transitions with λ_{max} = 330 and 528 nm.[125] As in nitroxy-radicals, the $n-\pi^*$ state is responsible for the photochemical activity of DPPH.

Presumably, on $n-\pi^*$ excitation a possible mechanism of the photochemical destruction of DPPH is one involving the abstraction of hydrogen from solvent molecules. This hypothesis has been confirmed by a series of investigations. Thus, on photolysis of DPPH in methyl methacrylate (MMA) and in MMA solution in benzene in the absence of oxygen, the radical is quantitatively converted into the corresponding hydrazine[129]. The reaction kinetics obey the first-order equation with respect to the radical and MMA and can be described schematically as follows:

$$\text{DPPH} \xrightarrow{h\nu} (\text{DPPH})^*$$

$$\text{DPPH}^* \xrightarrow{f+d} \text{DPPH (deactivation)},$$

$$\text{DPPH}^* + \text{M} \xrightarrow{r} \text{DPPH} - \text{H} + \dot{\text{M}}(\text{P}) \text{ (reaction)},$$

$$\text{DPPH} + \dot{\text{M}}(\dot{\text{P}}) \xrightarrow{k} \text{DPPH} - \text{H} + \text{products (disproportionation)}.$$

Here $\dot{P}$ is the macroradical obtained by the addition of the $\dot{M}$ radical to the monomer. At 25°C $(f + d)/r$ = 2.3 ± 1.1 M, i.e. the quantum yield of the reaction and the reactivity of the excited radical are high.

In the presence of O_2 the reaction kinetics are more complicated: DPPH is destroyed in a zero-order reaction and hydrazine is formed only in small amounts; radical oxidation and decomposition products have been found. Evidently in the presence of oxygen the reactions of DPPH involving MMA peroxy-radicals play a significant role[129].

The photolysis of DPPH in various hydrocarbons has been investigated[130]. The destruction of the radical in the absence of oxygen obeys first-order kinetics and only light corresponding to the 330 nm bond is photochemically active. The rate constant ratio $(f + d)/r$ and the quantum

yields (φ) at 25°C are presented in Table 5. Evidently the quantum yields are fairly high; there is also a correlation between the quantum yield and the energy of the C–H bond dissociated in the hydrocarbons. The rate-limiting stage of the reaction is the abstraction of a hydrogen atom by the excited radical.

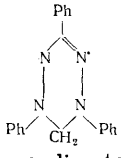
Table 5. The quantum yields of the photochemical destruction of DPPH.[130]

Solvent	$(I+d)/r$	Φ
Hexane	4.71	0.18
Toluene	3.16	0.24
Cyclohexane	2.70	0.27
Methylcyclohexane	1.77	0.36
Cumene	0.66	0.59

DPPH-H is also formed on irradiation of DPPH with light corresponding to the long-wavelength absorption band in acetic acid, in an ethanol–acetone mixture[131], in carbon tetrachloride, and in benzene[132].

3. Triphenylverdazyl

The triphenylverdazyl (TPV) radical



is excited by light corresponding to the absorption bands with λ_{max} = 400 and 710 nm. Both bands are intense ($\epsilon \simeq 10^4$ litre mole^{-1} cm^{-1}); being displaced towards the red in polar solvents, they probably correspond to $\pi-\pi^*$ transitions[133]. The lowest $\pi-\pi^*$ state is probably responsible for the photochemical activity of TPV. The dipole moment of TPV in the excited state, determined from the spectroscopic shifts of the 400 nm band in various solvents, is 9 D, i.e. on photoexcitation the dipole moment of the radical increases by about 6 D.[133,134]

The principal pathways for the photochemical destruction of TPV involve the abstraction of a hydrogen atom from the solvent with formation of the corresponding leuco-base and also the dissociation of the N–N bond with formation of the five-membered ring of 1,3-diphenyl-1,2,4-triazole and aniline.

It has been established that concentration-dependent quenching of the radicals takes place, i.e. the higher the concentration of the radical the slower the photochemical reaction. The quantity $k_q\tau \simeq 5 \times 10^3$ litre mole^{-1} was determined from the kinetic curves for the destruction of the radicals at their different concentrations. The rate constant for the diffusional encounters of radicals can be determined from the concentration-dependent broadening of the ESR line. It is caused by the exchange interaction of the electrons of the colliding radicals[125]. The rate constant for the collisions found from the exchange broadening of the ESR lines is 1×10^9 litre mole^{-1} s^{-1}, i.e. is close to the rate constant for diffusional collisions. If it is assumed that this constant is identical with the quenching constant k_q, then the lifetime of the excited state of the radical is found to be unduly long: $\tau = 5 \times 10^{-6}$ s. On the other hand, if it is assumed that the lifetime of the excited radical is 10^{-7}–10^{-8} s, then k_q is found to be 10^{10}–10^{11} litre mole^{-1} s^{-1}, i.e. exceeds by two–three orders of magnitude the value corresponding to the diffusion-controlled process. Possibly the concentration-dependent quenching is not associated with the diffusion of radicals, but proceeds via an inductive-resonance mechanism. However, an unambiguous choice between these two situations is impossible on the basis of the data quoted above.

4. The Perchlorotriphenylmethyl Radical (TPM)

The stable radical $(C_6Cl_5)_3\dot{C}$ has an absorption spectrum consisting of four bands with maxima at 220 nm ($\epsilon = 1 \times 10^5$), 293 nm ($\epsilon = 7 \times 10^3$), 382 nm ($\epsilon = 7 \times 10^4$), and 510 and 562 nm ($\epsilon = 10^3$ litre mole^{-1} cm^{-1}). Each band is photochemically active[135].

The principal pathway to the photochemical destruction of the radical involves the abstraction of a hydrogen atom from solvent molecules with formation of the corresponding triphenylmethane. The effective rate constants for the destruction of the radical in various solvents are different; there is an approximate correlation between the energies of the C–H bonds dissociated in the solvents and the radical destruction rate constants.

In the photolysis of TPM in the presence of aromatic additives the electronically-excited state of the radical is found to be quenched by these additives. This can occur via two mechanisms: firstly in a charge-transfer complex (since all the additives are effective electron donors) and secondly via energy transfer.

5. π-Complexes and Hydrogen Bonds Involving Electronically Excited Radicals

Data have been obtained for the π-complexes of excited radicals and for hydrogen-bonded complexes[136]. The difference between their heats of formation of the ground (ΔH_g) and excited (ΔH_e) states can be obtained from a thermodynamic cycle involving the excited radical[137]:

$$\Delta H_g - \Delta H_e = h(\nu_0 - \nu_s),$$

where ν_0 and ν_s are the frequencies at the maxima of the electronic bands of the radical in inert and solvating solvents.

The solvation mechanism is as follows:

$$\dot{R} + S \overset{K_g}{\rightleftarrows} \dot{R}_s \quad ,$$
$$\dot{R}^* + S \overset{K_e}{\rightleftarrows} \dot{R}_s^* \quad ,$$

where K_g and K_e are the equilibrium constants for the solvation of the radical in the ground and excited states.

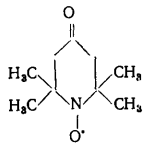
Then

$$\ln K_e/K_g = \frac{\Delta H_e - \Delta H_g}{RT} = \frac{h(\nu_0 - \nu_s)}{RT} \quad , \qquad (27)$$

provided that the entropies of the ground and excited states are identical. The ratio of the equilibrium constants for the solvation of the ground and excited states and the difference between the activation energies for the decomposition of the solvated states can be determined from the spectral shifts by Eqn. (27).

It was found that the formation of a π-complex by the dianisylnitroxy-radical with benzene causes a bathochromic shift of the absorption band in the electronic spectrum of the radical (λ_{max} = 329 nm in heptane and λ_{max} = 336 nm in benzene). $\Delta H_e - \Delta H_g$ = 1.3 kcal mole^{-1} can be found from the shift by Eqn. (27). Thus the π-complex of the excited radical (excimer) is more stable to the extent of 1.3 kcal mole^{-1} than the π-complex of the radical in the ground state[136].

Analysis of the hypsochromic shifts of the $n-\pi^*$ absorption band of aliphatic nitroxy-radicals permits the calculation by Eqn. (27) of the equilibrium constant for association via hydrogen bonding in the excited $n-\pi^*$ state of the radical. It was found that for the radical



$K_e/K_g = 2.9 \times 10^{-3}$ in methanol and $K_e/K_g = 2.5 \times 10^{-4}$ in acetic acid (at 22°C). Thus the equilibrium constant for solvation in the excited $n-\pi^*$ state of the radical is much smaller than in the ground state; accordingly, the solvate of the ground state is much more stable than that of the excited state.

Thus electron transfer from the n orbital of oxygen to the excited π^* molecular orbital weakens the donor–acceptor interaction in the hydrogen-bonded complex and displaces the solvation equilibrium towards the free radicals. Since the lifetime of the excited state is much longer than the vibration period of the nuclei in the hydrogen bond bridge, on excitation the radical may be involved in further reactions as a free non-associated species. This result is of significant importance for the kinetics of the reactions of radicals in the electronically excited state.

IV. THE QUENCHING OF EXCITED STATES BY RADICALS

The deactivation of electronically excited states of molecules by paramagnetic species is of considerable interest to spectroscopists and photochemists; because in the presence of paramagnetic quenching agents different quenching mechanisms operate from those of quenching by diamagnetic molecules; this is caused by the removal of the spin prohibition of electronic transitions in the excited molecule in the presence of paramagnetic species. For example, oxygen is known to be an excellent quenching agent for excited singlet and triplet states. Nitric oxide possesses similar properties. Since for the majority of organic molecules energy transfer to NO is impossible, evidently effective quenching of this molecule involves a reorientation of the electron spin in the excited molecule, but the total spin of the system is retained:

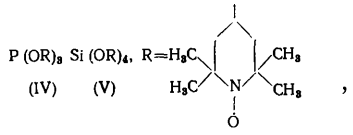
$$^3M(\uparrow\uparrow) + {}^2NO(\uparrow) \rightarrow {}^1M(\downarrow\uparrow) + {}^2NO(\downarrow),$$

where ^3M denotes the triplet state of the molecule, ^1M the ground singlet state, and the arrows indicate the orientations of the electron spins. This mechanism was first proposed by Porter and Wright[138].

However, oxygen and nitric oxide are not always suitable quenching agents, since they are frequently actively involved in chemical reactions and alter their mechanisms. This naturally led to interest in other paramagnetic quenching agents (metal ions and complexes and organic, especially stable, radicals). In this section the quenching of excited states by organic radicals will be considered.

1. The Quenching of Excited States in a Liquid

The quenching of the fluorescence of 2,5-diphenyloxazole, anthracene, 1,2-benzanthracene, and naphthacene in cyclohexane by the radical (I) and the polyradicals (IV) and (V),



was observed by Buchachenko et al.[139] The kinetics of the quenching process obeyed the Stern–Volmer equation and the ratio of the quenching constants for the radical (I) (k_q) and oxygen (k_{O_2}) was 0.53, 0.57, 0.53, and 0.73 respectively for the above electron donors. Evidently, the rate of quenching of excited singlet states is limited by the diffusion of the species. The fluorescence of rubrene and rhodamine B, where the position of the excited singlet level coincides with that of the radicals, was not quenched. Hence it was concluded that the quenching of the excited singlet state of donors occurs only if this state is above the lowest excited level of the quenching radical, i.e., in other words, the quenching by radicals involves energy transfer via an exchange-resonance mechanism.

However, in a later study[140] the quenching of fluorescence by di-t-butylnitrogen oxide (t-$C_4H_9)_2NO$ (VI) was investigated in methylcyclohexane and measurements were made of the lifetime of the excited singlet states and the quenching rate constant; it was shown that both rubrene and rhodamine B are quenched almost as effectively as other donors with high singlet levels. The energies of the excited singlet states and the quenching rate constants are listed in Table 6.

Table 6. The energies of the excited singlet levels and the rate constants for quenching by the radical (V) and oxygen.

Donor	$10^3 E_S$, cm^{-1}	$10^{-9} k_q$, litre mole^{-1} s^{-1}	k_q/k_{O_2}
Naphthalene	32.2	8.2	—
Chrysene	27.7	8.5	3.9
Pyrene	26.9	7.8	3.2
Anthracene	26.7	12.9	2.4
1,2-Benzanthracene	26.0	8.0	3.5
9,10-Diphenylanthracene	25.5	9.2	3.5
Perylene	23.0	12.0	2.4
Naphthacene	21.2	6.4	3.8
Rubrene	18.5	2.1	5.6
Rhodamine B	17.5	4.7	—

Clearly the rate of quenching is diffusion limited and there is no unambiguous relation between the energy of the singlet level (E_S) and the quenching constant k_q. Hence it follows that energy transfer is not the principal quenching mechanism, i.e. the conclusion of Buchachenko

et al.[139] was incorrect. (They did not measure the lifetime of the singlet states τ_S; possibly the quenching of the fluorescence of rubrene and rhodamine B could not be observed owing to the short lifetimes of the excited donors.) One must also rule out quenching due to energy transfer via an inductive-resonance mechanism, since the efficiency of quenching is independent of the overlapping of the absorption bands of the donor and acceptor.

The mechanism of the quenching of excited singlet states $^1M^*$ as a result of a chemical electron transfer reaction with formation of ion pairs is possible:

$$^1M^* + \dot{R} \rightarrow (M^{\cdot-}\dot{R}) \rightarrow {}^1M_0 + \dot{R} \ .$$

Quenching by amines usually involves this mechanism, the quenching efficiency depending strongly on solvent polarity. The quenching has been found to depend[140] only on the viscosity of the solvent, i.e. quenching by the radicals (VI) does not take place via the charge transfer mechanism.

The most probable quenching mechanism involves the removal of spin prohibition in the contact complex ($^1M^*...\ ^2R$), which results in the induction of $S-T$ transitions in the excited molecule and relaxation of the excess energy in the vibrational degrees of freedom (this mechanism will be discussed in detail a little later).

The quenching of the singlet states of fluorenone by the radical (VI) with a diffusional rate constant was observed in a study of the photocycloaddition of fluorenone to ketenimine[141].

The radical (VI) also quenches the fluorescence of pyrene monomers and excimers in benzene solution with nearly diffusional rate constants: 8.4×10^9 and 4.1×10^9 litre mole^{-1} s^{-1} for the monomer and excimer respectively[142]. The rate constants for the quenching of the excited singlets of substituted benzenes by nitric oxides are also the same as the collision rate constants and hardly differ from the constants for the quenching by oxygen[143].

We shall now consider the quenching of triplet states by radicals. Yang and Murov[144] observed that the ketyl radicals formed in solutions in the photochemical reduction of benzophenone behave as quenching agents for triplet states. In a study of photocycloaddition of fluorenone and aromatic aldehydes to olefins and ketenimine[145,146] it was found that the radical (VI) quenches both the singlet and triplet states of fluorenone with a diffusional rate constant. The quenching of triplet exciplexes by the radical (VI) has been observed in a study[147] of the photoaddition of 2-cyclohexenes to 1.1-dimethoxyethylene. In the radiolysis of mixtures of benzene and but-2-ene in the presence of the stable galvinoxyl radical (a phenoxy-radical) excited benzene triplet molecules are quenched[148]. $k_q\tau = 4.8 \times 10^2$, where k_q is the quenching rate constant, close to a diffusional constant (about 5×10^9 litre mole^{-1} s^{-1}) and τ is the lifetime of the triplet benzene molecule. It has been shown[149] that the *NNN'N'*-tetramethyl-*p*-phenylenediamine radical-cation (Wurster's cation) is an effective quenching agent for the triplet states of anthracene molecules. Thus the lifetime of the triplet state of anthracene in methylene chloride solution is 2.8×10^{-6} s in the presence of 1.8×10^{-7} M cation and 6.4×10^{-6} s in the absence of the cation.

It is interesting that in a magnetic field (up to 7000 G) the rate of quenching falls, i.e. the magnetic field inhibits the quenching of the triplet states of molecules by radicals. This inhibition also explains the increase in the intensity of the phosphorescence of the triplet molecules of aromatic hydrocarbons obtained in electrochemical reactions[150]. In this case the electrochemically generated hydrocarbon radical-anions are oxidised by Wurster's radical-cation with formation of triplet states of aromatic molecules. With increase of the magnetic field strength, the electroluminescence intensity rises; this effect can be explained by the fact that the magnetic field inhibits the quenching of the triplets by Wurster's cation.

Incidentally, the influence of the magnetic field on the efficiency of the quenching of the triplets is evidence that the quenching does not occur in every collision between the excited molecule and the quenching agent, i.e. that the rate of quenching is lower than the rate of diffusional collisions. This conclusion was confirmed quantitatively in two investigations[151,152]. The quenching of benzophenone and stilbene triplets by the radical (VI) takes place with a rate constant close to the diffusional value ($\sim 3 \times 10^9$ litre mole^{-1} s^{-1}), while the triplet state of naphthalene is quenched much more slowly (6×10^8 litre mole^{-1} s^{-1}). The perdeuteronaphthalene triplet is quenched still more slowly (3.7×10^8 litre mole^{-1} s^{-1}).[151] Thus the probability of quenching on collision with a paramagnetic species also depends significantly on the probability of the intramolecular radiationless degradation of the excitation energy (cf. naphthalene and deuteronaphthalene).

An interesting dependence of the rate constants for the quenching of triplets of aromatic molecules by the radical (VI) and nitric oxide on the energy of the triplet levels has been observed[152]. With increase in the energy of the triplet level, the rate constants initially decrease and then rapidly increase; the constant has a minimum corresponding to the energy $\sim 14 \times 10^3$ cm^{-1}. Both quenching agents behave in exactly the same way, although the energies of their lowest excited levels differ markedly. The observed relations have been explained by the hypothesis that quenching takes place in charge-transfer collision complexes; however, this hypothesis involves certain difficulties, since it does not explain the identical efficiencies of both quenching agents and is not consistent with the effect of the dielectric constant on the quenching efficiency.

Table 7. The quenching rate constants and the energies of the triplet levels of donors.

Donor	$10^{-8}k_q$, litre mole^{-1} s^{-1}	E_T, kcal mole^{-1}
Stilbene	50	48
Diacetyl	37	55
Benzophenone	26	69
Fluorenone	15	53
Biphenyl	7	69
Phenanthrene	6.4	62
Naphthalene	6.3	61
3-Acetylphenanthrene	6.0	59
1-Bromonaphthalene	5.2	59
Naphthalene-d_8	3.7	60

The quenching of triplets by the radicals (VI) has been investigated in detail[153]. Table 7 presents the quenching rate constants and the energies of the triplet levels. Evidently there is no unambiguous relation between the constants k_q and the position of the triplet level. However, there is a definite tendency as regards quenching efficiency: stilbene is quenched most effectively, $(n-\pi^*)$-excited triplets of ketones are quenched less effectively,

and the efficiency of the quenching of the $\pi-\pi^*$ triplets of aromatic hydrocarbons is lowest. This trend and the absence of a correlation between k_q and E_T constitute powerful evidence against the quenching mechanism involving energy transfer.

The exchange-induced quenching mechanism appears to be the most likely. It involves the removal of spin prohibition and the induction of the reorientation of the electron spin in the excited triplet in the contact complex of the excited molecule and the radical $^3M...R$ as a result of the exchange interaction of the electrons:

$$^3M^* + \dot{R} \rightarrow (^3M\cdots\dot{R}) \rightarrow {}^1M_0 + \dot{R} \ .$$

This process can be called exchange-induced vibrational relaxation rather than energy exchange, since the energy remains in the same initial molecule and is then degraded via its vibrational levels[154]. Evidently the probability of such vibrational relaxation depends on the exchange interactions in the contact complex $^3M...R$ and must be sensitive to the details of the electronic interactions in the complex and to the nature of the electron orbitals involved in complex formation.

The physical validity of this quenching mechanism was recently confirmed from completely different standpoints. In a study of the NMR of various organic molecules in the presence of stable radicals it was observed that even in the ground state all the molecules are involved in complex formation with the radicals[155]. In these short-lived complexes the unpaired electron of the radical is transferred to the orbitals of the molecules involved in the complex, i.e. there is partial merging of the electron shells and formation of common molecular orbitals. The nature of the complexes is extremely varied, but they can be classified in terms of the type of orbitals involved in complex formation ($n-\sigma$, $\pi-\sigma$, $\pi-\pi$, $\pi-n$, etc.) Here n, σ, and π are the orbitals of the lone pairs and σ bonds and π orbitals.

There is no doubt that radicals form complexes of this type with excited molecules and the electronic interactions in these complexes determine the efficiency of the quenching by radicals of excited states such as singlet and triplet states.

2. The Quenching of Excited States in the Solid Phase

Ern and Merrifield[156] showed that the triplet excitons of anthracene are quenched by the radicals formed when crystalline anthracene is irradiated by X-rays. The quenching of the phosphorescence of tetrahydrocarbazole and benzophenone by the radicals (I) in mixtures of alcohol and ether frozen at 77 K has been observed[157]. In the presence of the radicals there was merely a decrease of the intensity of the phosphorescence, while the kinetics of the decrease did not change after switching on the exciting light, i.e. the lifetime of the triplet state was independent of the presence of the quenching radicals and of their concentration. This shows that the quenching proceeds via the mechanism proposed by Perren[158], who suggested that the molecule of the quenching agent creates around itself a sphere of action of specific volume, so that the excited molecule is instantaneously quenched when it enters this sphere; on the other hand, when the molecule is outside the sphere of action of the quenching agent, it luminesces as an unperturbed molecule, i.e. in the same way as in the absence of the quenching agent.

This model yields the following expression for the dependence of the intensity (or quantum yield) of the phosphorescence on the concentration of the quenching agent c:

$$I/I_0 = \exp(-vNc) = \exp(-\alpha c),$$

where I_0 is the phosphorescence at $c = 0$ and $N = 6 \times 10^{20}$ mol. cm^{-3} (when v is expressed in cm^3 and the concentration is on the molar scale). Having determined experimentally the variation of I with c, it is possible to find from this equation the volume v of the sphere of action of the quenching agent.

The radius of the sphere where tetrahydracarbazole is quenched by the radical in alcohol–ether mixtures, determined in this manner, is 10 ± 1 Å, the value for benzophenone being 12.9 ± 0.8 Å. Thus the Perren radii for the quenching of the triplet states of electron donors by nitroxy-radicals are close to the radii corresponding to quenching by the usual molecules[157].

The radiolysis of the stable nitroxy-radical 2,2,6,6-tetramethyl-1-piperidinyloxy-radical has been investigated[159] in a pure form (in the absence of extraneous molecules) and in solid solutions of the radicals in isopropyl alcohol.

After the irradiation of individual radicals in the temperature range 100–300 K, the latter are destroyed by a first-order reaction with a rate constant k proportional to the dose rate γ:

$$N = N_0 e^{-kt} = N_0 e^{-k_1 \dot{\gamma} t} = N_0 e^{-k_1 D},$$

where D is the radiation dose. The constant k_1 obeys the Arrhenius relation with an activation energy of about 0.4 kcal $mole^{-1}$; the values of k_1 are 4×10^{-4} Mrad at 100 K and 1.4×10^{-3} $Mrad^{-1}$ at 300 K.

In the radiolysis of radicals in solid solutions in isopropyl alcohol (at a concentration of 2.4×10^{19}–2.5×10^{20} radicals g^{-1}) the constant k_1 is much higher, amounting to 4×10^{-2} $Mrad^{-1}$. Thus in solid solutions the radicals are destroyed by radiation with a high radiation yield—about 240 radicals are destroyed for 100 eV of the energy absorbed by the radicals; the radiation yield of the destruction of the radicals derived from isopropyl alcohol is much lower: 2–3 radicals for 100 eV. The high efficiency of the radiolytic destruction of stable radicals shows that in the solid state the radicals behave as powerful acceptors of the energy of excited states arising on γ-irradiation. However, the physical causes of such quenching remain unknown.

The influence of radicals on the quenching of excited singlet and triplet states of aromatic amines (diphenylamine, triphenylamine, and carbazole) in solutions frozen at 77 K has been studied[160]. If the radicals in the matrix were obtained photochemically, then an increase of the radical concentration entailed a parallel decrease of the intensity of both the fluorescence and phosphorescence of the amines. Hence it was concluded that the radicals quench the excited singlet states. If the radicals were obtained by the radiolysis of solid solutions, then the quenching efficiency was an order of magnitude lower. In other words, in order to quench the phosphorescence of amines to the same extent, the concentration of the radicals generated by radiation must exceed by an order of magnitude the concentration of the photochemically generated radicals.

This interesting effect was explained[160] by the characteristics of the distribution of the radicals: in photolysis the radicals are generated and located near amine molecules, i.e. there is a high local concentration of the

quenching agent near the molecules being excited, while in radiolysis the distribution of radicals is much more uniform. Nevertheless, even in radiolysis it is not ideally uniform. Indeed, when the Perren radii for quenching by "radiation" radicals are determined, they are found to be about 30–35 Å. They are physically unreal, since the overlapping of the absorption bands of the electron donor and the quenching agent is weak and the inductive-resonance mechanism cannot ensure such effective quenching. The distribution of radicals in space during radiolysis is probably also non-uniform[160].

Table 8. The types of excitation and chemical reactions of radicals.

Excitation	Radicals	Type of reaction	Excitation	Radicals	Type of reaction
$\pi-\sigma^*$	Alkyl	Decomposition	$\sigma-\pi^*$	$R\dot{C}O$	Decomposition
$\pi-\pi^*$ (?)	Alkyl	Substitution (?), isomerisation	$\pi-\pi^*$	Allyl	Substitution
				Polyenyl	»
$\pi-\sigma^*$	$\dot{C}H_2OH$	Decomposition		Triphenylverdazyl	»
	$R\dot{C}HOMe$	»		Perchloro-triphenylmethyl	»
	$\dot{C}H_2COMe$	»	$n-\pi^*$	Nitroxyl	»
	$\dot{C}H_2C(=O)OH$	»		Diphenylpicryl-hydrazyl	»
	$\dot{C}H_2C(=O)OC(=O)CH_3$	»		$R\dot{O}_2$	Substitution, decomp. (?)
	$MeC\dot{H}N(C_2H_5)_2$	»	$n-\pi^*$	Perchlorotriphenyl-methyl	Electron transfer
			$\pi-\pi^*$	Wurster's cation	ditto

Thus radicals are effective quenching agents for excited singlet and triplet states also in the solid phase. The quenching mechanism is probably the same as in the liquid and consists in the exchange-induced removal of spin prohibition and the subsequent vibrational relaxation of the energy of the excited molecule.

V. CONCLUSION

Despite a number of difficulties and ambiguities in the interpretation of the results of experimental studies on the reactions of excited radicals, definite advances have been made in the development of this field. Thus a definite relation has been noted between the nature and type of excitation of the radical and the mode of its reaction; it can be observed in the analysis of the compilation in Table 8.

It is readily seen that the radicals with $\pi-\sigma^*$ or $\sigma-\pi^*$ excitation mainly decompose (alkyl radicals, radicals derived from alcohols, ethers, ketones, carboxylic acids, their anhydrides, and amides, acyl radicals, etc.). In all these cases the σ orbitals of the radicals are involved in excitation; decomposition at the β-bond (for example, $\dot{C}H_2OH \rightarrow CH_2O + H^{\cdot}$) or at the α-bond (for example, the decomposition of acyl radicals and probably alkyl radicals) is most characteristic under these conditions.

The radicals with $\pi-\pi^*$ or $n-\pi^*$ excitation are mainly involved in reactions with transfer of a hydrogen atom (allyl, polyenyl, peroxy, and nitroxy-radicals, DPPH, etc.). Finally, radicals with a low ionisation potential (perchlorotriphenylmethyl) are involved in electron transfer on excitation.

Admittedly the relations noted above are only approximate and qualitative, but they nevertheless show that the transformations of excited radicals are not unduly varied and that there is a definite system in their behaviour. In many instances quantitative characteristics were also found: the quantum yields of the reactions have been determined and the lifetimes of the excited radicals and the quenching constants have been measured; the changes in the dipole moments of a number of radicals on excitation, due to the rearrangement of the electron shell, have been determined.

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Ions and Ion-pairs in Nucleophilic Aliphatic Substitution

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A survey is made of the involvement of ions and ion-pairs formed both by the nucleophilic reagent and by the substrate. Evidence is given for the existence of ion-pairs of different types (contact and solvent-separated) in S_N1 reactions, and the possible participation of the former type in S_N2 processes is examined. A list of 338 references is included.

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I. INTRODUCTION

A most important current problem of theoretical organic chemistry is the involvement not only of covalent molecules but also of various ionic intermediates, free ions, and different types of ion-pairs in the reactions of organic compounds. These species change significantly the reactivity of the substrate and the mechanism of the reaction. The participation of carbonium ions in nucleophilic substitutions is based on evidence of the mechanism of unimolecular substitution (S_N1), first put forward by Ingold and his coworkers [1], and whose classic formulation presupposes the formation of a steady concentration of a free ion in the rate-determining stage of the reaction. Later, nucleophilic substitutions involving stable carbonium ions were studied. A vast amount of information has now accumulated on the role and the reactivity of free ions (carbonium ions [2] and carbanions [3,4]), but special attention has been paid during the past decade to the fact that these species are frequently present in solution and take part in a reaction not in the free state but associated with their gegenion. The "ion-pair" concept, well known in the chemistry of electrolytes [5], was introduced into organic chemistry by Winstein (on Grunwald's suggestion).

As early as 1960 Winstein wrote: "It is important to distinguish between ionisation and dissociation, and to consider explicitly the role of different ionic intermediates, representing various stages of ionisation and dissociation" [6]. The idea that ionic intermediates other than the carbonium ion might be present during nucleophilic substitutions occurred to him after he had established that solvolysis in allylic systems is accompanied by intramolecular rearrangement of the initial compound [7]. Proof of the existence of such ionic intermediates, which it was proposed to term "ion-pairs" (internal and external, but in present-day literature contact or intimate and solvent-separated or loose), was obtained from many studies not only of allylic isomerisations but also of rearrangements in systems containing a 2-arylethyl group, from a comparison of rates of solvolysis, racemisation, isotopic exchange in ArC*HXR systems, and randomisation in esters ROC^{18}OAr, and also from a study of salt effects. These results led to the idea [8] that a covalent compound dissociates into free ions in stages involving the formation of at least two types of ion-pairs, return from which may result in isomerisation of either the cationic or the anionic moiety of the molecule:

$$RX \rightleftharpoons \underset{\underset{R^+ + X^-}{\uparrow\downarrow}}{R^+X^-} \rightleftharpoons R^+ \,\Big\|\, X^- \rightleftharpoons R^+ + X^-$$

It was suggested that reactions of type S_N1 may involve not only free ions but also solvent-separated ion-pairs.

An attempt has been made during recent years to demonstrate that ion-pairs of contact type may take part in S_N2 reactions of non-activated secondary (and even primary) substrates, although efforts to suggest a "unified" mechanism of nucleophilic substitution encounter serious difficulties. However, the idea that a substrate reacts in various forms depending on structure and conditions, with all differences in mechanism determined by the relative rates of individual stages, is an extremely tempting approach. Thus evidence of the existence in solution not only of carbonium ions but also of different types of ion-pairs is based on an analysis of kinetic and stereochemical results.

A completely different situation became evident when the existence of ion-pairs was examined in the chemistry of carbanions. Physical investigations in this field, which has developed vigorously during recent years, have provided direct evidence of the existence of various types of ion-pairs in solutions of salts of carbanions and radical-anions [9]. Especially valuable studies were made by Weissman [10], who in 1958 was the first to obtain physical proof of the existence of ion-pairs from the electron spin resonance spectra of salts of radical-anions, after which further work showed the existence of two types of ion-pairs [11-13]; Smid and his collaborators [14-16] have demonstrated the existence of contact and solvent-separated ion-pairs in a study of the spectra of salts of carbanions. It was Smid's papers which attracted the special attention of organic chemists to this problem. By now it has become possible not only to identify the different types of ion-pairs but also to establish their physical properties, energetics, solvation, and dynamics [17].

The present situation is somewhat paradoxical in that ion-pairs of carbanions have been thoroughly studied by various physicochemical methods, but very little is known of their reactivity in electrophilic substitution [18-20], whereas ion-pairs of carbonium ions are widely enlisted to explain the rules of nucleophilic substitution, although

objective data on their structure are lacking. However, the immense successes achieved in connection with this problem in the chemistry of carbanions have overshadowed the achievements in the field of carbonium ions, although the actual concept of ion-pairs was formulated by Winstein precisely in application to carbonium ions and nucleophilic substitution. The present Review examines the evidence for the existence of ions and ion-pairs in S_N reactions and the role of ion-pairs in uni- and bi-molecular nucleophilic substitution.

II. IONS AND ION-PAIRS MX IN S_N2 REACTIONS

Among nucleophilic substitutions those involving ionic nucleophilic reagents are some of the most important, both practically and theoretically. Here a special position is occupied by the exchange of halogens $RX-X^-$, termed the Finkelstein exchange [1]. The reactivity of the anions—their nucleophilicity in these reactions—is determined by the electronegativity, polarisability, and solvation, which in turn depend on the nature of the reaction centre under attack, the leaving group, and the solvent.

An important factor determining the reactivity of an ion, which for a long time was not taken into account, is the ability to associate with a gegenion [5], which is especially marked in media of low dielectric constant. With incomplete dissociation of the ionophore [21] the reaction rate constant will fall as its concentration increases. This phenomenon has been observed for quite a long time with halogen salts. Thus in 1948–1949 Evans et al. [22,23] discovered that the second-order rate constant for the reaction of n-butyl bromide with lithium bromide in acetone at 25°C decreases by a factor of 3.6 with increase in the lithium bromide concentration by a factor of 400, and explained this on the hypothesis that the reactant species was the bromide ion. A similar observation was made at that time by Moelwyn-Hughes in a study of the reaction of methyl bromide with potassium iodide in acetone [24].

Table 1. Relative RX + Hal^- reaction rate constants.

RX*	Solvent**	Cl⁻	Br⁻	I⁻	Ref.
n-PrBr	acetone	11	5	1	27
n-BuOBs	acetone	16	4	1	27
MeOTs	DMF	9.1	3.4	1	28
MeOTs***	83.3Py-DMF	2.8	1.5	1	29
EtOTs	HMPA	14 4	2.0	k_2 M^{-1} min^{-1}	30

*Bs = p-$SO_2C_6H_4Br$; Ts = p-$SO_2C_6H_4CH_3$.
**DMF = dimethylformamide; Py = pyridine; HMPA = hexamethylphosphoramide.
***K_{eq} was obtained from the kinetic data.

In many later papers, however, the degree of dissociation of the salts was disregarded, with a consequent distortion of the true reactivity of the halide ions [25]. In work on the Finkelstein exchange in $RHal-Hal^-$ systems in acetone Ingold et al. [26] observed in 1955 that the reaction rate constant increases with decrease in the lithium halide concentration, which they attributed to a negative salt effect. They regarded this as confirmed by the diminution in rate on the addition of lithium perchlorate, actually due to suppression of dissociation of the lithium halide. The reaction sequence of halide ions obtained by these workers—$I^- > Br^- > Cl^-$—was analogous to that observed in water and protonic media [25], which for a long time was considered an effect of polarisability varying in the same sequence. However, Winstein et al. [27] recalculated these results taking into account the degree of dissociation of the lithium halide, and found that the reaction sequence of halide ions in aprotic solvents was exactly the opposite, and the observed nucleophilicity diminished in the sequence $Cl^- > Br^- > I^-$ (Table 1). The ion-pair $\rightleftharpoons$ ions equilibrium constant increases in this sequence in acetone, but depends in general on the nature of the solvent [31]. The results obtained by Winstein et al. [27] show that the difference in reactivity between lithium and tetrabutylammonium halides towards n-butyl p-bromobenzenesulphonate in acetone is determined solely by the difference in their dissociation (Table 2). If the degree of dissociation is ignored, the true reactivity sequence for the reaction of methyl toluene-p-sulphonate in a mixture of pyridine and dimethylformamide is reversed when the salt concentration is increased to 0.35 M. [29]

Table 2. Observed and true rate constants for reaction of n-butyl p-bromobenzenesulphonate with lithium and tetra-n-butylammonium halides.

Salt	10^4K_{diss}	10^3k_{obs}, M^{-1} s^{-1}	$k_2 = 10^3k_{obs}/\alpha$, M^{-1} s^{-1}
n-Bu_4NCl	22.8	33.5	58
LiCl	0.027	0.493	51
n-Bu_4NBr	32.9	9.09	13
LiBr	5.22	2.81	12
n-Bu_4NI	64.8	1.68	2.0
LiI	69	2.97	3.6

Inspection of available results shows that salts of alkali metals with various anions are strongly associated into ion-pairs in ambipolar aprotic solvents [31,32], and neglect of this effect distorts the results significantly. With lithium bromide in acetone, for example, the order of the reaction with respect to the nucleophile is distorted [33]. For the reaction of 1-iodo-2,4-dinitrobenzene with potassium iodide in acetone [34] disregard of association to ion-pairs leads to an apparent change in the mechanism from S_N2 to S_N1.

It is no less important for the assessment of true reactivity to take into account the dissociation of alkoxides [35], wnich, in aprotic solvents such as dimethyl sulphoxide, are frequently used as nucleophiles in aromatic substitution and as bases in the elimination and generation of carbanions. Alkoxides are present in dimethyl sulphoxide predominantly as ion-pairs [35].

Crown polyethers have recently been used to increase the degree of dissociation of metal halides and alkoxides [36]. Addition to 18-crown-6 to a solution of potassium fluoride in acetonitrile increases sharply the observed nucleophilicity (and basicity), leading e.g. to ready substitution of fluorine for bromine in benzyl bromide [37]. Potassium ethoxide in the presence of dicyclohexyl-18-crown-6 is able to intervene in nucleophilic aromatic substitution, converting o-dichlorobenzene into o-chloroanisole in 40–50% yield [38]. In the presence of a crown polyether the nucleophilicity of the acetate ion is sharply increased, and

alkyl derivatives AlkX (where X = Cl, $OSO_2C_6H_4CH_3$, and especially Br) are readily converted into acetates [39]. Addition of a crown polyether has a similar influence on the reaction of alkyl halides with the cyanide ion [40].

It was accepted in most of the studies, however, that a free ion was the active species in nucleophilic substitution, and that the contribution by ion-pairs to the reactivity could be neglected, i.e. that $k_i \gg k_{ip}$ and that $k_{obs} = \alpha k_i$. Nevertheless, this contribution $(1 - \alpha)k_{ip}$ may be comparable with the contribution by the free ion αk_i if dissociation of the salt is slight ($\alpha \ll 1$) even when $k_i \simeq 10k_{ip}$. During recent years several workers [41-50], notably Beronius, have used Acree's equation [51] to estimate the reactivity both of free ions and also of ion-pairs in nucleophilic substitutions involving halides:

$$k_2 = \alpha k_i + (1-\alpha)k_{ip}; \qquad K_{eq} = \frac{c_\alpha^2 f_\pm^2}{1-\alpha},$$

where k_i is the reaction rate constant of the free ion, k_{ip} that of an ion-pair, α the degree of dissociation, $f_\pm$ the activity coefficient of the ion, and K_{eq} the equilibrium constant.

It was natural to expect that k_i would be independent of the nature of the cation, unlike k_{ip}. It has in fact been shown [27,50] that k_i has the same value for various cations. However, Lichtin et al. [41] did observe some dependence of k_i on the nature of the cation, with a regular increase in the ratio k_i/k_{ip} as K_{eq}^{-1} increased (Table 3). Although we usually find that $k_i \gg k_{ip}$, [50] the accompanying data show that the two rate constants may be comparable. Thus in the case of tetraethylammonium chloride $k_{ip} = \frac{1}{2}k_i$. In such cases, of course, it is not permissible to neglect the part played by ion-pairs and calculate $k_2 = k_{obs}/\alpha$, as is usually done [27,52-55].

Table 3. Rate constants for reactions of ions and ion-pairs of *p*-nitrobenzyl bromide with various bromides and chlorides.

MX	$10^5 k_i$, $M^{-1}\,s^{-1}$	$10^5 k_{ip}$, $M^{-1}\,s^{-1}$	$\frac{k_i}{k_{ip}}$	MX	$10^5 k_i$, $M^{-1}\,s^{-1}$	$10^5 k_{ip}$, $M^{-1}\,s^{-1}$	$\frac{k_i}{k_{ip}}$
p-$NO_2C_6H_4CH_2Br$+$M^{36}Cl$ in liq. SO_2, at 0°C				*p*-$NO_2C_6H_4CH_2Br$+ $M^{82}Br$ in liq. SO_2			
RbCl	2.69	0.076	35	KBr	7.89	0.38	21
Me_4NCl	2.92	0.47	5.2	Me_4NBr	7.24	1.07	6.8
Et_4NCl	3.17	1.61	1.97	Et_4NBr	7.07	2.86	2.5

Ion-pairs are the sole reactant species [42] in the reaction between 1-alkylpyridinium iodides and methyl toluene-*p*-sulphonate in chloroform, dichloroethane, and methyl formate. In solvents of high dielectric constant such as acetone and acetonitrile, however, ions and ion-pairs make comparable contributions to the observed rate-constants (e.g. for 4-cyano-1-ethylpyridinium iodide in acetonitrile k_i and k_{ip} have the respective values 0.175 and 0.12 $M^{-1}\,s^{-1}$).

For the reaction of *p*-nitrobenzyl chloride with lithium chloride in acetone the contribution by k_{ip} is <1% of that by k_i according to Beronius [43]; similarly, k_{ip} can be neglected in the reaction of n-butyl bromide with lithium bromide in acetone [45] or in a mixture of acetone with a large quantity of water [48]. When the lithium salts are replaced in these reactions by the corresponding tetrabutylammonium halides, however, the contribution by ion-pairs cannot be neglected in calculating the true rate constants, since k_{ip} amounts to 10% and 20% of k_i respectively. It was shown, in agreement with Lichtin's results [41?], that k_i is somewhat higher for lithium chloride than for tetrabutylammonium chloride (2.4 and 2.0 $M^{-1}\,min^{-1}$ respectively).

The complexity of determining the true value of k_i lies in the uncertainty attached to the salt effect. An attempted estimate by Beronius for the reaction of iodoalkanes with the iodide ion in aqueous ethanol [47] revealed that the assumption of minimum and maximum salt effects (on $f_{RX}f_{X^-}/f_{\neq}$) produced a marked change in k_{ip} from negative to large positive values of 30–50% of k_i.

It must be noted also that the values of K_{eq} calculated from electrical conductivity data, and hence the estimated contribution by ion-pairs, depend not only on the accuracy of the measurements (the conductivity of electrolytes in non-aqueous media has only recently been measured accurately) but also on the method of calculating them [56].

Considerable attention has been paid to the reactivity of ions and ion-pairs of ambident anions. Thus Smith et al. [57,58] determined the rate constants for the methylation of the ion and the sodium ion-pair of fluorenone oxime in a mixture of acetonitrile and t-butyl alcohol by methyl iodide, and found the ion to be more reactive than the ion-pair by a factor of 500.

It is especially interesting to estimate the true rate constant k_i and the contribution by ion-pairs in the reactions of ambident organic ions such as enoxide ions containing two nucleophilic centres joined by a single mesomeric system. Brändstrom showed [59] that both the ion and the ion-pair are kinetically active in the methylation of alkali-metal enoxides in alcohol†. A similar observation was made by Forsblad [60] in a study of the alkylation of alkali-metal methyl $o\beta$-dihydroxycinnamates. With the dipiperidinium bisenoxide in methanol the ion-pair was more active than the free ion in both *C*- and *O*-alkylation, probably because of selective solvation of the anion by hydrogen bonding. Thus the diminution in reactivity due to formation of a hydrogen bond may be greater than that resulting from electrostatic interaction with a gegenion of large radius and low charge density.

The most thorough study of the dual reactivity of ions and ion-pairs of ambident enoxide ions in alkylation has been reported in a series of papers [61-66]. At concentrations <0.1 M in hexametapol [hexamethylphosphortriamide, HMPT] the only reactive species is the "free" enoxide ion of acetoacetic ester [61] and other acyclic β-keto-esters [62], and its rate of alkylation by ethyl toluene-*p*-sulphonate parallels the basicity of the ambident anion. In a less basic medium such as dimethylformamide not only the ion but also ion-pairs of alkali-metal enoxides of acetoacetic ester take part in the reaction [63]. The rate constant of the reaction involving the anion was determined from experiments in the presence of macrocyclic polyethers. The greater reactivity of the ion-pair of sodium ethyl acetoacetate than of the potassium enoxide definitely indicates that the solvent-separated form of the ion-pairs of alkali-metal enoxides undergoes alkylation in dimethylformamide. In the presence of a crown polyether in such a weakly polar and feebly basic medium as dioxan [64], and even in the more strongly basic tetraglyme [65], contact ion-pairs of alkali-metal enoxides of acetoacetic ester take part in the reaction. This conclusion is based on the excellent linear

† Alkylation of an enoxide ion at a carbon atom can be regarded not only as an S_N2 reaction but also as an S_E reaction, and this field overlaps the study of carbanionic reactions.

correlation between $\lg k_{ip}$ and the reciprocal of the crystallographic radius of the cation—a relation that is typical of contact ion-pairs.

It is interesting that the stereochemical results of the *O*-alkylation of alkali-metal enoxides of acetoacetic ester depends on the nature of the ionic species involved [66], since the ion and the solvent-separated and contact ion-pairs may have different conformations.

III. PROOFS OF THE EXISTENCE OF CARBONIUM IONS IN S_N1 REACTIONS

Proofs of the existence of carbonium ions in nucleophilic substitutions are usually based on study of the kinetics and the stereochemistry of an S_N1 type of reaction. The classic theory of such reactions requires that the observed constant should be independent of the concentration and the nature of the nucleophile [1]:

$$RX \underset{k_1,\ \text{slow}}{\overset{}{\rightleftharpoons}} R^+ + X^- \xrightarrow[k_2,\ \text{rapid}]{N^-} RN;$$

$$w = \frac{k_1 k_2 [RX][N^-]}{k_{-1}[X^-] + k_2[N^-]};$$

when $k_2[N] \gg k^{-1}[X^-]$, we have $w = k_1[RX]$. Such regularities have been observed in the reactions of t-butyl bromide with various nucleophiles in nitromethane [67-69].

Another criterion of the involvement of carbonium ions in reactions is the "common-ion effect" [70-76] (the mass-action effect" or, as defined by Winstein [7], "external return"), depression of the observed constant on introduction of a common ion or on its accumulation during the reaction. The mechanism of the effect involves return of the ion as a result of reaction with the gegenion to form the initial compound, and operates when the contribution $k_2[N^-]$ is comparable with $k_{-1}[X^-]$. The common-ion effect is the more strongly developed the more stable is the resulting carbonium ion [71,77-81]. The common ion is thus acting as a nucleophilic "trap" for the carbonium ion. A foreign nucleophile such as the azide ion may be used as ionic trap, and would not affect the rate of the process but would influence the composition of the products, since the rate-determining stage in S_N1 processes does not coincide with the stage governing the products formed:

$$RX \underset{\text{slow}}{\rightleftharpoons} X^- + R^+ \begin{cases} \xrightarrow{HOS^-} ROS \\ \xrightarrow{N^-} RN \end{cases}.$$

Precisely this result was obtained for the reactions of di- and tri-phenylmethyl derivatives with sodium azide and tetrahydroborate used as traps [72-74,82-86].

Use of a nucleophilic trap combined with change in the nature of the leaving group provides another indication of formation of a carbonium ion in S_N1 reactions:

$$\left.\begin{matrix} RCl \\ RBr \end{matrix}\right\} \rightleftharpoons R^+ \begin{cases} \xrightarrow{HOS^-} ROS \\ \xrightarrow{N^-} RN \end{cases}.$$

Thus the reaction of diphenylmethyl chloride and bromide with the azide ion in 90% aqueous acetone yielded mixtures of the same products, although the reaction velocities of these halides differed thirty-fold [74,82].

An important criterion of formation of a carbonium ion is the stereochemical result of the reaction: a racemic product formed from an optically active compound undoubtedly indicates an S_N1 mechanism [1]. Because of the participation not only of free ions but also of ion-pairs in reactions of S_N1 type, however, the stereochemistry of these processes may in general be extremely diverse, as will be seen later, varying from substantial inversion to complete retention of the stereochemical configuration.

Finally, mention may be made of a further criterion, which is especially significant for diagnosing the mechanism of solvolytic reactions and consists in the influence of structural effects on the reaction velocity.

Schleyer et al. [87] recently proposed the addition of sodium azide as a test for the mechanism of solvolytic reactions. It is quite clear that, if the reaction velocity is unaffected by such addition, the solvent, being the weaker nucleophile, is incapable of nucleophilic participation in the rate-determining stage, i.e. that the reaction takes place by an S_N1 mechanism.

With sufficiently stable carbonium ions an S_N2C^+ mechanism [68] is possible, when the carbonium ion is formed in the pre-equilibrium stage and reacts slowly with the nucleophile: $k_2[N] \ll k_1[X^-]$. This probably occurs most often in the reactions of triphenylmethyl derivatives. However, such reactions may involve not only free ions but also ion-pairs, whose concentration in the solution may not be stationary, since these compounds may already be present in an ionised and partly dissociated state.

IV. IONS AND ION-PAIRS IN SOLUTIONS OF TRIPHENYLMETHYL DERIVATIVES

In strongly acid solutions even carbonium ions such as isopropylium, which are classified as unstable, can exist for a long time [88]. The more stable triarylmethyl cations are formed in theoretical yield by the action of sulphuric acid on the corresponding carbinols, and are entirely stable in these solutions [89]. Carbonium ions can be obtained from triarylmethyl derivatives also in other media or in the presence of Lewis acids [90].

In less strongly ionising media a covalent compound is in equilibrium with ion-pairs, as is shown by spectral investigations. Thus according to Evans [91] triphenylmethyl chloride dissolved in nitromethane and other nitroalkanes does not dissociate but merely undergoes ionisation (in nitromethane $K_{ion} \simeq 4 \times 10^{-4}$); tri-*p*-tolylmethyl chloride behaves similarly in nitrobenzene [92]. In dichloroethane solution triphenylmethyl chloride is capable only of ionisation ($K_{ion} \simeq 7.9 \times 10^{-3}$), whereas tri-*p*-tolylmethyl chloride undergoes partial dissociation [93]. The establishment of two equilibria in this case follows from the linearity of the plots of $([R^+] + [R^+Cl^-])/[RCl]$ against $([RCl])^{-1/2}$. In fact

$$RCl \overset{K_1}{\rightleftharpoons} R^+Cl^-;$$

$$R^+Cl^- \overset{K_2}{\rightleftharpoons} R^+ + Cl^-;$$

$$RCl \overset{K_3}{\rightleftharpoons} R^+ + Cl^-;$$

$$K_3 = \frac{[R^+]^2}{[RCl]} = K_1 K_2;$$

$$\frac{[R^+] + [R^+Cl^-]}{[RCl]} = K_1 + \frac{[R^+]}{[RCl]} = K_1 + K_3 \frac{1}{\sqrt{[RCl]}}.$$

Triphenylmethyl bromide is assumed to be completely dissociated in *m*-cresol solution [94]; the degree of dissociation is diminished by the addition of benzene or hexane to the *m*-cresol [95]. Dissociation is increased in chlorinated ethanes compared with nitroalkanes, but no direct relation is observed between the dissociating or ionising power of a solvent and its dielectric constant [93]. Liquid sulphur dioxide is a good ionising solvent, in spite of its low

dielectric constant (ϵ = 15.4 at 0°C).[96,97] Solutions of triphenylmethyl chloride in liquid sulphur dioxide conduct electricity, and comparison of spectral and conductivity data[98] permitted calculation of the ionisation constant and of the constant of dissociation of the ion-pair into free ions (K_1 = 0.013 and K_2 = 0.003 M at 0°C)[99,100]. Liquid sulphur dioxide is a stronger ionising solvent that nitrobenzene by a factor[97] of 5×10^{10} ($K_1 = 2 \times 10^8$ and 0.004 respectively).

It has recently been shown[101] that the ionisation of triphenylmethyl chloride in ether, assessed from the rate of isotopic exchange with $*Cl^-$, is promoted by lithium perchlorate, which in this solution forms aggregates of diverse structure. The dissociation and ionisation of triarylmethyl halides is increased by complex formation with Lewis acids[90,102]. The influence of salts on these processes diminishes in the sequence[103]

$$SbCl_5 \gg FeCl_3 \gg SnCl_4 \gg BiCl_3 > HgCl_2 > SbCl_3 .$$

The complexes $(XC_6H_4)_3CCl.HgCl_2$ (where X = H, *p*-Cl, *p*-CH_3) in nitromethane undergo not only ionisation but also dissociation[104,105], and the bromides dissociate still more readily under these conditions[106]. Similar results were obtained in other solvents[105]. Spectroscopic results indicate that solvents form the sequence—nitromethane > chlorobenzene > benzene—according to their ability to ionise the complex; the ability of a solvent to solvate both the anion and the carbonium ion must, of course, be taken into account, as well as the possibility of variation in the extinction coefficient of the carbonium ion under the influence of solvation[107]. Furthermore, the ratio of dissociated to covalent form may change during the reaction as a consequence of the common-ion effect[108].

Increase in ionicity on passing from triarylmethyl halides to the perchlorates is indicated by conductivity data[109-111] and by the absorption spectra[112,113]. Triethyl perchlorate is completely ionised and partly dissociated in chlorinated solvents—chloroform, dichloromethane, and the dichloroethanes[114].

The presence of ions and ion-pairs in a solution of tropylium isothiocyanate

$$RNCS \rightleftharpoons R^+NCS^- \rightleftharpoons R^+ + NCS^-$$

has been demonstrated by nuclear magnetic resonance[115]. The ratio between the covalent form and the ionic species depends on the composition of the solvent and the temperature. Thus in trideuteroacetonitrile only free ions are formed, whereas in its mixture with deuterochloroform (1 : 3) at 40°C ion-pairs are also present.

In order to describe the reactivity of dissociating and ionising organic compounds it is necessary to estimate separately the contributions made by each of the reactant species, as in the case of metal halides.

In media of low dielectric constant nucleophilic substitutions can take place in the triarylmethyl series by an S_N1 mechanism, when dissociation (or ionisation) occurs in the limiting stage, and ions and ion-pairs are present in steady concentrations. Nucleophiles capable of forming a hydrogen bond with the leaving group may assist the ionisation; since they may be associated in these media, their observed kinetic order is complicated[99,116-118]. At one time this and other complications connected with the return mechanism gave rise to bitter controversy between Ingold et al.[119-123] and Swain et al.[124-128]. Kinetic complications may arise also from aggregation of the ion-pairs[129,130].

It may be assumed that in these media the S_N1 mechanism involves only the formation of solvent-separated ion-pairs. This hypothesis is supported by the absence of depression of the rate constant by the common ion in the methanolysis of diphenyl-*p*-tolylmethyl toluene-*p*-sulphonate in a mixture of oxolan and methanol (10%), and by the considerable acceleration of this reaction on the addition of lithium perchlorate[131].

A considerable number of studies have now been made on the reactivity of free triarylmethyl cations. They originally covered the most stable amino-substituted triarylmethane dyes, whose rates of reaction were not very high[132-135]. However, application of the stopped-flow method extended considerably the range of carbonium ions investigated[136-140]. Study of the effect of additions of salts on the reaction of triarylmethyl cations with water[141,142] showed that variation in the rate was due to association of the carbonium ion with the anion of the added salt, in particular to formation of ion-pairs with the perchlorate anion.

A special position among this work is occupied by Ritchie's superb investigations[143-150], which included a study of reaction rates and equilibria for triarylmethyl and also substituted tropylium and benzenediazonium ions with various nucleophiles in several solvents. Unusual results were obtained, which have not yet been fully explained. This work showed firstly that the "stability–reactivity" principle breaks down. Although the required opposition between the stability of an ion pK_{R^+}[151] and its rate of reaction with nucleophiles was observed in a series of ions, Brønsted's equation was on the whole inapplicable, and in several cases no correlation was evident between the logarithms of rate and equilibrium constants. Absence of correlation was also mentioned earlier between $\lg k$ for the reaction of triarylmethyl cations with water and pK_{R^+} with variation in the number of *para*-substituents from 1 to 3.[136] However, a "reactivity–stability" correlation was observed in the hydride reduction of triarylmethyl cations[137,138].

Secondly, Ritchie discovered the surprising fact that carbonium ions differing considerably in stability had the same selectivity. The distribution of products of competing S_N1 reactions had shown that the selectivity of a carbonium ion towards nucleophiles depended on its stability. In 1966 a linear relation‡ was found[152] for a series of S_N1 reactions between $\lg k_1$ and $\lg(k_N/k_S)$ (where k_N and k_S are the reaction rate constants with the azide ion and with water respectively; the ratio $k_N[N_3^-]/k_S$ can be found from the distribution of the reaction products $[RN_3]/[ROH]$. This relation was extended by Schleyer et al.[153] and by Harris et al.[154].

Ritchie's results show that the rate of reaction of a carbonium ion increases with the nucleophilicity of the other reactant, but the ratio k_N/k_S remains almost constant for all the carbonium ions investigated. The reactions of substituted tropylium ions with hydroxide ions and with water may be cited as examples (Table 4). Although reactivities varied by 10^2, and stabilities by $10^{2.5}$, the k_{OH^-}/k_{H_2O} ratios were very closely similar[143]. A possible explanation[155] is that the reaction velocity is governed by desolvation of the nucleophile, which is independent of the cation.

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‡ It must be borne in mind that a linear dependence may be distorted by the return mechanism, although it is supposed[154] that the fractional return is small in aqueous ethanol, in which the correlation was obtained.

The quantity $N_+ = \lg(k_N/k_{H_2O})$, where k_N is the reaction rate constant in a given solvent and k_{H_2O} the rate constant for reaction of the same cation with water in pure water, was proposed[147] as a measure of the nucleophilicity of the nucleophile N in the solvent. The nucleophilicity sequence thus obtained, quite apart from the absolute values, differed very markedly from published results determined in relation to other substrates[156-159].

Table 4. Comparison of stability of substituted tropylium ions with their reactivity towards OH^- and H_2O.

Cation	pK_{R+}	k_{H_2O}, s^{-1}	k_{OH^-}, $M^{-1}s^{-1}$
$C_7H_7^+$	4.76	2.6	$3.1\cdot10^5$
$C_6H_5C_7H_6^+$	4.86	1.0	$7.9\cdot10^4$
p-$ClC_6H_4C_7H_6^+$	4.55	1.2	$1.4\cdot10^5$
p-$CH_3C_6H_4C_7H_6^+$	5.75	0.27	$4.0\cdot10^4$
p-$Me_2NC_6H_4C_7H_6^+$	6.90	0.02	$1.7\cdot10^3$

Dorfman et al.[160] have recently obtained unique data on the reactivity of the benzyl cation. They used pulsed radiolysis to generate benzylium from various benzyl derivatives, and to determine rate constants for its reactions with methanol, ethanol, and the bromide and iodide ions as ($k_2^{24°}$, $M^{-1}s^{-1}$) respectively 7.4×10^7, 1.3×10^8, 5.2×10^{10}, and 4.9×10^{10}.

V. PROOFS OF THE EXISTENCE OF ION-PAIRS IN S_N1 REACTIONS

1. Special Salt Effect

An attempt to test the possible involvement of various types of ionic intermediates in solvolytic reactions led Winstein et al. to undertake a series of studies of salt effects in the solvolysis of sulphonates and halides[8,161-170]. In the normal salt effect additions of such a salt as lithium perchlorate, not containing a common ion, produce an increase in the titrimetrically determined solvolysis rate constant: $k_t = k_t^0(1 + b[\text{Salt}])$, where b is a measure of the normal salt effect. Such a relation has been observed in the solvolysis of several primary and even secondary systems in aqueous acetone and in acetic acid[161,164]. In some cases, however, the introduction of small quantities of lithium perchlorate produced a sharp increase in reaction velocity (Fig. 1). This phenomenon was termed a "special salt effect" and was observed e.g. with *o*- and *p*-methoxyphenethyl toluene-*p*-sulphonates in alcoholic acetic acid[162] and with *trans*-2-*p*-methoxyphenyl-cyclopentyl and -cyclohexyl *p*-bromobenzenesulphonates, *p*-methoxy-α-methylphenethyl toluene-*p*-sulphonate, *erythro*-*p*-methoxy-$\alpha\beta$-dimethylphenethyl *p*-bromobenzenesulphonate[163], and 2,4-dimethoxyphenethyl toluene-*p*-sulphonate in acetic acid[165]. With further increase in the lithium perchlorate concentration only the normal salt effect was observed in conformity with the equation $k_t = k^0_{ext}(1 + b[LiClO_4])$, so that the special salt effect is defined by the ratio k^0_{ext}/k^0_t (Fig. 1).

Winstein and his coworkers suggested that the solvolytic product ROS could be formed from the carbonium ion or from the solvent-separated ion-pair, and return to the covalent form could take place at all stages—external ion return k_{-3} involving the anion X^- and hence depending on its concentration, external ion-pair return k_{-2}, and internal ion-pair return k_{-1}:

$$\underset{(I)}{RX} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{(II)}{R^+X^-} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \underset{(III)}{R^+\|X^-} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \underset{(IV)}{R^+ + X^-}$$
$$k_S^{III}\downarrow HOS \qquad k_S^{IV}\downarrow HOS$$
$$ROS \qquad ROS$$

It was assumed also that exchange of anions could occur only by means of a solvent-separated ion-pair, which would be converted into a different, more reactive ion-pair, with suppression of the return stage k_{-2}:

$$R^+\|X^- + M^+\|Y^- \rightleftharpoons R^+\|Y^- + M^+\|X^-$$

(exchange involving the ion-pair $M^+\|Y^-$), and

$$R^+\|X^- + Y^- \rightleftharpoons R^+\|Y^- + X^-$$

(exchange involving the ion Y^-). However, the effect of lithium perchlorate on the ratio k_1/k_{-1} corresponds to the normal salt effect.

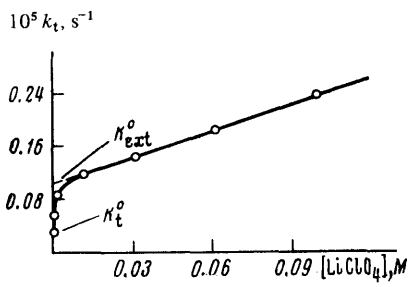


Figure 1. Typical dependence of solvolysis rate constant on $LiClO_4$ concentration in presence of a special salt effect. The points represent values of k^0_t, and the broken line indicates k^0_{ext}.

Thus the action of lithium perchlorate consists in the usual "chemical capture", which, unlike capture by other nucleophiles (N^-), does not yield a stable compound RN but a well ionised compound formed in solution by a reactive ionic intermediate. This mechanism of the action of lithium perchlorate is confirmed by the suppression of the special salt effect on addition of a salt having a common ion, e.g. lithium toluene-*p*-sulphonate in the reaction of an alkyl toluene-*p*-sulphonate[166] because of competition for the ion-pair (III). It is noteworthy that lithium toluene-*p*-sulphonate exhibits a positive salt effect in the acetolysis of *p*-methoxy-α-methylphenethyl toluene-*p*-sulphonate. The absence of depression of k_t by the toluene-*p*-sulphonate anion suggests absence of a return stage involving the free ion, i.e. an intramolecular return stage.

Depression of the constant by a common ion may in principle be absent in two cases—(i) with very reactive ions, for which $k_S^{IV} \gg k_{-3}$ and (ii) when a solvolytic reaction involves only a loose ion-pair ($k_S^{III} \gg k_3$). In several

other reactions, e.g. in the acetolysis of *p*-methoxy-α-methylphenethyl or norbornyl toluene-*p*-sulphonate, the addition of lithium toluene-*p*-sulphonate led to a decrease in the solvolytic constant[168]. An exhaustive kinetic analysis by Winstein et al. yielded a formula for the titrimetric solvolysis constant in the absence of a common-ion effect ($k_{-3}[X^-] = 0$) and with complete depression ($k_{-3}[X^-] \gg k_S^{IV}$). Under certain conditions this method permits not only detection of ion-pairs but also quantitative calculation of the fractional return at different stages.

Winstein repeatedly emphasised that the presence of a special salt effect proves the existence of return stages, but a return mechanism is possible even in the absence of a special salt effect.

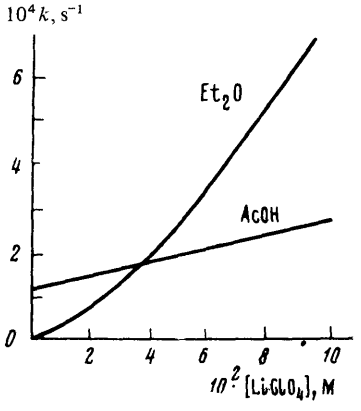


Figure 2. Dependence of ionisation rate constant for *p*-methoxy-$\beta\beta$-dimethylphenethyl toluene-*p*-sulphonate on the concentration of lithium perchlorate in diethyl ether and in acetic acid.

The bromide ion can also function as a trap for a solvate-separated ion-pair[167]. Formation of a bromo-derivative from *p*-methoxy-$\alpha\beta$-dimethylphenethyl *p*-bromobenzenesulphonate and *p*-methoxy-α-methylphenethyl toluene-*p*-sulphonate in acetic acid is a first-order reaction, and the exchange is subject to a normal salt effect.

Especially large salt effects are observed in slightly polar and weakly ionising media. Acetic acid, in which most of the studies of salt effects have been made, is a weakly polar but quite strongly ionising solvent[169,170]. The rate of ionisation of *p*-methoxyneophyl [*p*-methoxy-$\beta\beta$-dimethylphenethyl] toluene-*p*-sulphonate in ether increases on addition of 0.1 M lithium perchlorate by the immense factor of 10^5 (in acetic acid and in diethyl ether *b* has the respective values 12.2 and 298 000).[169] At a certain concentration of the lithium salt (>0.036 M) ether becomes a more strongly ionising medium than is acetic acid (Fig. 2). In solvents of this type it is supposed[170] that the added salt, present as an ion-pair, coordinates with the substrate to form a quadrupole:

$$RX + M^+Y^- \rightleftharpoons [R^+X^-M^+Y^-]$$

and such electrophilic assistance promotes the ionisation of RX.

The use of lithium perchlorate in poorly dissociating solvents may lead to distortions of the dependence $\lg k = f([LiClO_4])$. This may be responsible for the criticism of Winstein's work resulting from a study of the effect of additions of salts on the rate of reaction of triphenylmethyl chloride with methanol in benzene[171] which disregarded the dissociation of the added tetrabutylammonium chloride and perchlorate.

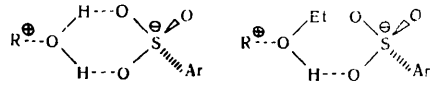
2. Distribution of Products in Competing Reactions. Nucleophilic "Traps" for Ion-pairs

Effect of leaving group

One method already noted for demonstrating the existence of a carbonium ion is the use of nucleophilic "traps", which affect the composition of the products without changing, in the case of a classic S_N1 process, the reaction velocity[2,74,83]. Competition between a strong nucleophile and the solvent for an ionic intermediate is expressed by a competition factor[172], which is easily determined from experimental data on the yield of products: $F_N = k_N/k_S = [RN]/[ROS][N]$, where F_N increases with the stability of the cationic intermediate[152,153,173]. For an unstable carbonium ion, exhibiting poor selectivity, the factor F_N should approach unity.

As already mentioned, one test for an S_N1 mechanism is that F_N should be unaffected by the nature of the leaving group. Thus the ratio $[RN_3]/[ROH] = 1.94$, the same for the reactions of diphenylmethyl chloride and bromide in aqueous acetone[74]. However, F_N depends§ not only on the nature of R in RX but also on that of the leaving group[175], which suggested that certain S_N1 reactions involve not the free carbonium ions but ion-pairs.

Thus the alkene/alcohol ratio in the reaction of t-butyl derivatives depends on the nature of the leaving group[176]. This result, may, of course, be due to partial involvement of an S_N2 mechanism. Variation in selectivity depending on the leaving group has been observed also in the reaction of 2-adamantyl arenesulphonates in aqueous alcohol[177]. The ROC_2H_5/ROH ratio diminished with increase in stability (with rise in $\lg k$), although the opposite relation might have been expected with attack on a free carbonium ion, in view of the great nucleophilicity of ethanol. Ion-pairs



are assumed to be involved in the reactions, and of these the pair separated by a water molecule is the more stable. The nature of the leaving group has a considerable effect on $F_N = k_{N_3^-}/k_{H_2O}$ in the reactions of triphenylmethyl chloride and bromide in 80% acetone[175]. The yield of hydrocarbon relative to that of the alcohol increases on passing from the chloride to the bromide in the reactions of diphenylmethyl and especially 1-phenylethyl halides with sodium tetrahydroborate in aqueous diglyme[178]. The

§ Detailed analysis[174] of various effects on the competition factor (not only by the structure of the substrate, the nature of the leaving group, and the nucleophile but also by the medium, the temperature, and even the rate of stirring) shows that a cautious approach must be made to comparing values obtained in different investigations.

leaving group has been found to affect the composition of the solvolysis products in the reactions of cyclobutyl arenesulphonates [179].

The selectivity factor in the solvolysis of triphenylmethyl chloride (0.013 M) in the presence of sodium azide (0.039 M) in 95% aqueous dioxan changed sharply on the addition of lithium nitrate and especially perchlorate [180] (0.089 M $LiClO_4$ increased [ROH]/[RN_3] from 20.2/79.8 to 41/59), which can be regarded as an argument in support of the formation from $R^+\|Cl^-$ of the more stable and less selective ion-pair $R^+\|ClO_4^-$. However, another possible explanation [180] is the influence of the ionic strength on the rates of the two "product-determining" reactions and the greater retardation by the salt effect of the ion–ion reaction (of the triphenylmethyl cation with the azide anion) than of the ion–dipole reaction (of this cation with water).

Comparison of stability of ion-pairs based on competitive substitution

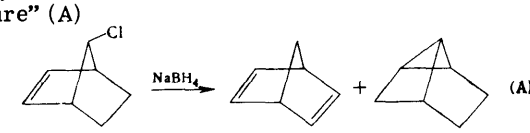
The solvolysis of 1,1- and 3,3-dimethylallyl [3-methylbut-2-enyl] chlorides yields mixtures of primary and tertiary alcohols, which suggests a common ionic intermediate. However, the action of sodium tetrahydroborate in aqueous ethanol results in different ratios (12.0 and 6.25) of the hydrocarbons $(CH_3)_2C:CH.CH_3$ to $CH_2:CH.CH(CH_3)_2$. [181] This difference is not due to simultaneous reaction by mechanisms S_N1 and S_N2 or S_N2', since doubling the concentration of sodium tetrahydroborate produces no significant change in these ratios. Hence it may be concluded that ion-pairs of similar but not identical structure are formed: i.e. they are distinguished by charge delocalisation in the cationic component, which is significant for attack by the hydride ion.

An interesting comparison was made [182] of reactivities and product compositions in the hydrolysis in aqueous diglyme of cyclopropylmethyl (V) and cyclobutyl (VI) methanesulphonates and of their 1-methylated derivatives in the presence of sodium tetrahydroborate or sodium azide. The reactivity of (V) was almost tenfold that of (VI), but the alcohols formed were almost identical in composition—almost equal quantities of (V)–OH and (VI)–OH with a little allyl alcohol. The suggested that a common intermediate was formed in the limiting stage, which might be a "non-classical" bicyclobutonium ion. However, the competition factors $F_N = k_N/k_{H_2O}$ (N = BH_4^-, N_3^-) were different, larger for (V)¶. Furthermore, different ratios of hydrocarbons are formed also with sodium tetrahydroborate: the ratios of methylcyclopropane to cyclobutane obtained on reaction with (V) and (VI) are respectively 3 and 2. Hence the reaction involves not a free carbonium ion but an ion-pair, having similar but not identical structures with (V) and (VI). Reactivity and selectivity data indicate that the ion-pair of (V) is more stable than that of (VI): i.e. a primary pair is more stable than a secondary pair. The same conclusion is reached from a study of competition factors for 1-methylated (V) and (VI): introduction of the methyl group diminishes selectivity, so that, in contrast to the free carbonium ions, the selectivity (and probably the stability) of the ion-pairs diminishes in the sequence—primary > secondary > tertiary.

An analogous relation has been found [174] for the sulphonates and halides of several "classical" systems for the study of S_N1 processes. However, it was noted that ambiguity was associated with use of the F_N criterion for assessing the mechanism in the intermediate region, where results could be interpreted in terms either of competition between S_N1 and S_N2 mechanisms or of the ion-pair S_N2 mechanism suggested by Sneen [183], since in this case the relation between competition factor and structure might be quite complicated.

Nucleophilic "traps" for ion-pairs

The use of lithium tetrahydroaluminate in ether as a nucleophilic trap for the "non-classical" carbonium ion in the reaction of 7-chloronorbornadiene led to the formation not only of norbornadiene but also of a "non-classical structure" (A)



which was regarded [184] as formed from a contact ion-pair, since it is difficult to assume an S_N1 mechanism in this solvent or S_N2 attack by a hydride ion on the double bond.

An interesting "trap" for ion-pairs in the reactions of diphenylmethyl and *p*-chlorodiphenylmethyl chlorides in 80% acetone is cobalt(II) nitrate [185]. Since this salt greatly affects the rate of solvolysis but has no effect on the polarimetric constant, it was deduced that racemisation involves ion-pairs of the same type (probably contact), while "capture" involves solvent-separated ion-pairs.

3. Stereochemistry

Comparison of rates of racemisation, solvolysis, and isotope exchange

The idea of the participation of ion-pairs and the occurrence of a return stage in solvolytic processes of S_N1 type were used by Winstein et al. [186] to explain the difference between the rate constants for loss of optical activity and for the solvolytic reaction of *exo*-norbornyl *p*-bromobenzenesulphonate ($k_\alpha > k_t$). These workers discovered a rule, which has since been confirmed: the fractional return increases as the nucleophilicity of the solvent decreases (Table 5). With $\alpha\beta$-dimethylphenethyl toluene-*p*-sulphonate as example it was shown [187] that the "excess" of racemisation was due to return of an ion-pair, not of the free ions, since the addition of sodium toluene-*p*-sulphonate hardly affected the ratio k_α/k_t, which had the respective values 2, 4.5–5, and 1.18 in ethanol, acetic acid, and formic acid. In the solvolysis of *threo*-*p*-methoxy-$\alpha\beta$-dimethylphenethyl *p*-bromobenzenesulphonate the ratio varies from 4.1 in acetic acid to 16 in a mixture of 10% of formic acid with dioxan [188]. Both constants increase on the addition of lithium perchlorate in conformity with the equation for the salt effect, in which $b_\alpha = 16.2$ and $b_t = 21.6$.

An analogous proof of the existence of ion-pairs in the reactions of dimethylphenyl systems is based on comparing k_α (determined polarimetrically) with k_t or the rate

¶ It is significant that the rate of reaction in the presence of sodium azide varies little, only a slight positive salt effect being observed, which does not support an S_N2 mechanism.

constant k_e for exchange between the halides and a radioactive halide ion. Thus the rate of loss of optical activity by the compounds $C_6H_5CHClC_6D_5$ and $C_6H_5CDClC_6D_5$ exceeds the aggregate rate of solvolysis and exchange with the radioactive chloride ion[189]: k_α/k_t has the values ~3, 20, and 100 in 50% acetone, nitromethane, and liquid sulphur dioxide respectively.

Table 5.

Solvent	AcOH	EtOH	75% Acetone
k_α/k_t	3.45	2.94	1.40

Winstein and his coworkers[6,190-195] made a series of determinations of the constants k_α, k_t, and k_e using *p*-chlorodiphenylmethyl chloride in various aprotic and other solvents. Values of the constants obtained by extrapolating to zero salt concentration were compared. Table 6, which lists the dielectric constants of the solvents together with the values obtained for the rate constants and the ratio k^0_α/k^0_e or k^0_α/k^0_t, shows that $k_\alpha > k_t$ or k_e in all the solvents, i.e. that the rate of return exceeds the rate of chemical capture. The value of k_α is strongly dependent on the ionising power of the solvent. It is interesting that a linear dependence of $\lg k^0_\alpha$ on $\lg k_1$ for the solvolysis of *p*-methoxy-$\beta\beta$-dimethylphenethyl toluene-*p*-sulphonate was obtained[196] for all six solvents at 75°C: $\lg k^0_\alpha = 4.22 + 2.02 \lg k_1$.

Table 6. Effect of solvent on the constants k^0_α, k^0_t, and k^0_e and their ratios for the reaction of *p*-chlorodiphenylethyl chloride with the chloride ion.

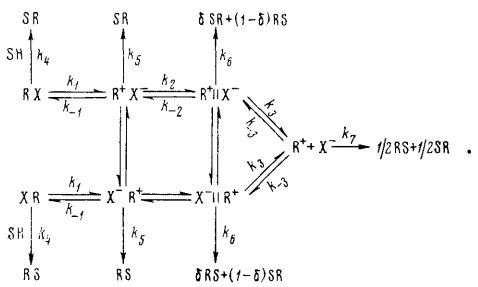
t, °C	Solvent	ε	$10^6 k^0_\alpha$, s^{-1}	$10^6 k^0_t$, s^{-1}	$10^6 k^0_e$, s^{-1}	k_{2e}**, $M^{-1}\,s^{-1}$	k^0_α/k^0_t	k^0_α/k^0_e
25	AcOH	6	68	1.8	—	—	38	—
25	80% CH_3COCH_3	30	60	23.1	—	—	2.6	—
75	CH_3NO_2	37	145	—	3.25	1.03	—	44
11	CH_3CN	37	60.7	—	0.2	1.23	—	304
11	$HCONMe_2$	37	18.9	—	5.0	2.00	—	4
11	CH_3COCH_3*	21	1.38	—	0.03	1.90	—	50

*Both processes, characterised by k_α and k_e, are slightly accelerated by lithium salts (chloride and perchlorate) and very strongly accelerated by the corresponding tetrabutylammonium salts, but their ratio varies little.
**The rate constant k_{2e} for bimolecular exchange with covalent RCl is found as the slope of the dependence of k_e on [MCl] at a low concentration of the isotopically labelled salt: $k_e = k^0_e + k_{2e}[(C_4H_9)_4NCl]$. The value of k_{2e} is almost the same in all solvents.

The ratio of the constants (k^0_α/k^0_t or k^0_α/k^0_e), of course, represents the ratio of the lower limit of the rate of ionisation to the rate of chemical capture, since part of the return may occur with retention of stereochemical configuration. As already noted, this ratio is strongly dependent on the nature of the solvent and decreases with increase in its nucleophilicity. For solvolytic reaction this occurs as a consequence of increase in the rate constant k_N for reactions of the ion-pair with the solvent. Initial attack on the pair $R^+\|X^-$ by a solvent molecule is assumed also for exchange, with formation of an intermediate that is more reactive in exchange, e.g. $RO.CH:N^+(CH_3)_2$ [or the less stable $CH_3C:N^+R$ and $(CH_3)_2C:O^+R$]. The results indicate that most of the ion-pairs in the majority of the ambipolar aprotic solvents used are converted back into the initial compound, and only a proportion of them undergo exchange.

Rates of exchange of chlorine and loss of optical activity have similarly been compared for the compounds $C_6H_5CHClCH_3$ and $C_6H_5CHClCH(CH_3)_2$ in various solvents[197]. In all cases k_α exceeds k_e, although their ratio is, of course, influenced by the variation in structure and solvent. Detailed investigation of the solvolysis of 1-phenylethyl chloride in 60% aqueous dioxan showed[198] that addition of lithium perchlorate produces a considerable increase in rate†, whereas lithium chloride has hardly any effect on the rate (k_α and k_t), which indicates an ionisation process, not dissociation. The ratio k_α/k_t remains almost unchanged: 1.18, 1.40, and 1.42 in the absence of additive and in the presence of 0.23 M LiCl and 0.23 M $LiClO_4$ respectively. An explanation was based[198] on Winstein's concept of equilibrium among various ionic intermediates, including solvated ion-pairs.

A similar relationship ($k_\alpha > k_t$) has been observed[199] in the solvolysis of 1-phenylethyl chloride in trifluoroethanol and in aqueous ethanol. Both solvent-separated contact ion-pairs, whose interaction with the solvent was accompanied by inversion, were regarded[199] as taking part. Thus the general scheme involves several equilibria and processes:



The results show that, of 100 contact ion-pairs in trifluoroethanol (97–100%), 80 undergo return, 18 are solvolysed (through solvent-separated ion-pairs), and 7 invert the configuration; the corresponding proportions in 60% ethanol are 70, 28, and 1.4.

Exchange in the systems comprising 1-phenylethyl chloride or bromide with the corresponding halide ions, as well as reactions with other nucleophiles, were studied by Pocker[200,201] in liquid sulphur dioxide and in nitromethane. Here, too, it was found that the rate of racemisation k_α exceeded the rate of exchange k_e together with the rate of the accompanying dehydrochlorination k_D.

† With *p*-chlorodiphenylmethyl chloride in 80% acetone k_t is larger in the absence of lithium perchlorate than in its presence in small concentrations: i.e. the dependence of the rate constant on the concentration passes through a minimum.

The ratio of return with racemisation to chemical capture was respectively 9 and 4 in the two solvents. However, as also with diphenylethyl bromide, a significant proportion of the exchange under these conditions took place by an S_N2 mechanism [202], when it was found that $k_{2\alpha} = 2k_{2e}$: i.e. every act of bimolecular exchange was accompanied by inversion of configuration, in conformity with theory.

The unimolecular racemisation rate constant for phenyl-*p*-tolylmethyl chloride in nitromethane exceeds the rate constant for reaction with various nucleophiles by a factor of 20 (in conformity with an S_N1 mechanism the same constant $k_1 \simeq 2 \times 10^{-7}$ was obtained at 0°C for various nucleophiles—the azide and chloride ions, pyridine, triethylamine [200]).

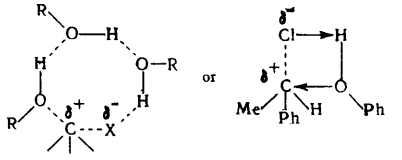
The involvement of ion-pairs in the "solvolysis" of s-butyl chloride in dimethylformamide in the presence of $Li^{36}Cl$ (the products are but-1- and but-2-ene and s-butyl formate) is also confirmed by comparing the rates of solvolysis, racemisation, and exchange [203].

Stereochemical "anomalies"

Various "anomalies" in the stereochemical results of unimolecular reactions are readily explained by the involvement of ion-pairs. Thus in several S_N1 solvolytic reactions inversion of configuration predominates over racemisation. For example, the methanolysis of 1-ethyl-1,3-dimethylbutyl phthalate, i.e. substitution at a tertiary carbon atom, is accompanied 54% by inversion and 46% by racemisation [204]. Such a result is usually attributed to shielding by the leaving group from nucleophilic attack, which in effect acknowledges the participation of ion-pairs in the reaction.

An analogous stereochemical effect of the leaving group, leading to predominant though not exclusive inversion, has been observed in the acetolysis of isomeric 4-t-butylcyclohexyl trifluoromethanesulphonates (triflates) (I). [204] The main product was an alkene, with only a certain quantity of acetates, inversion amounting to 94% for the equatorial compound and 75% for the axial compound. This suggested [205] that contact ion-pairs, not free carbonium ions, were involved in the reaction. The same conclusions had been reached earlier to explain incomplete inversion in the reactions of vinyl trifluoromethanesulphonates [206-208].

From the point of view of the mechanism and the possibility of the involvement of ion-pairs the greatest interest attaches to nucleophilic substitutions with retention of stereochemical configuration when this is not due to neighbouring-group participation but is a consequence of direct attack by the nucleophile [209,210]. A series of studies by Okamoto et al. [211-219] on the stereochemistry of the solvolysis of optically active 1-phenylethyl chloride showed extremely diverse results depending on the composition of the solvent. Thus solvolysis in the methanol–phenol–triethylamine system gave both products (of phenolysis and of methanolysis) with inversion of configuration when the initial phenol content has been 50% (by weight); from a phenol content of 85–95% both ethers exhibited complete retention of configuration; but in 75% phenol the methyl ether was formed with inversion, and the phenyl ether with retention [217]. A possible explanation suggested by Okamoto [217,218] was oriented coordination of attack by a solvent molecule on an ion-pair on the side of the leaving group. This explanation much resembles Cram's scheme [3] put forward to explain the retention of configuration at a carbanionic centre in reactions involving ion-pairs:



Retention of configuration can be explained also by differences between the uniform solvation of a carbonium ion and the possibly unsymmetrical solvation of an ion-pair on the side of the carbonium centre. If such solvation partly acquires the status of a bond, i.e. achieves directionality and some overlap of orbitals, though weaker than in nucleophilic attack‡, a situation may arise in which it is easier for the nucleophile to attack the carbonium centre from the direction of the leaving group than on the opposite side, which is shielded by a solvent molecule. Such a hypothesis was used to explain the partial retention of configuration in the reaction of optically active 2-bromooctane with the thiocyanate ion in dimethyl sulphoxide [220]. The considerable retention of configuration in the S_N1 reaction of *laevo*-biphenylyl-1-naphthylphenylmethyl benzoate in aqueous acetone, aqueous dioxan, and absolute alcohol was explained [221] on the same basis.

Retention of configuration by participation of the solvent was used by Okamoto [222] to explain the stereochemical result of the reaction of 1-phenylethyl chloride with a carboxylic acid in acetonitrile, when the fractional retention increased with the content of this solvent. Reaction was assumed to involve the "tail-solvated" ion-pair $CH_3CN...R^+...X^-$, in which the reaction centre interacts more strongly with the solvent than with the leaving group. However, the solvated ion-pairs considered here are not solvent-separated, and their involvement in the reaction presupposes that the S_N1 (or S_N2?) reaction may occur through another ionic intermediate, a solvated contact ion-pair. Solvation of an ion-pair from the "tail", as a result of which the reaction of 1-phenylethyl chloride with silver nitrate in diethyl ether takes place with retention of configuration, was considered also by Kornblum [223], but in acetonitrile the same reaction was accompanied by inversion; competition probably takes place between the solvent and the nitrate ion.

Complete retention of configuration was observed in the nucleophilic substitution of axial bromine in *trans*,*trans*-2-bromodecahydronaphthalene by the action of acetonitrile in the presence of silver perchlorate or tetrafluoroborate to give *N*-*trans*,*trans*-decahydro-2-naphthylacetamide [224]. Retention was observed in the solvolysis of menthyl toluene-*p*-sulphonate in aqueous alcohol (58%) and in trifluoroethanol (83%). [225]

There was a tendency [226,227] to explain the considerable retention of configuration in the acetolysis and the formolysis of *anti*-2,3-dideutero-7-norbornyl *p*-bromobenzenesulphonate (90% and 95% respectively) by frontal collapse of the ion-pair formed. An S_N1 mechanism is clearly indicated by the lack of effect of added sodium acetate on the stereochemical result of acetolysis. On the other hand, the lower percentage retention accompanying formolysis may be some argument that retention of configuration is not a consequence of the development of

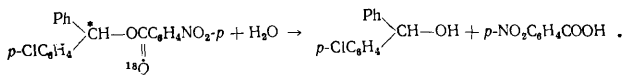
‡ This shows how blurred is the boundary between electrostatic solvation and formation of a covalent bond, leading to S_N1 and S_N2 mechanisms in solvolytic reactions.

synartesis and the formation of a non-classical carbonium ion. Thus reaction of a solvate-separated ion-pair and exchange in it of an anion without change in configuration provide yet another possibility. In other words, it must be supposed that attack on a contact ion-pair that is not solvated at a carbon atom takes place from the "tail", for exchange of an anion in a solvent-separated pair occurs at the front. However, the possibility of explaining retention of configuration by "non-classical" participation cannot be completely excluded[228].

Thus steric orientation is considerably more ambiguous in S_N1 than in S_N2 reactions, and can be explained only in terms of ion-pairs.

4. Isomerisation of Anionic Component

A powerful method for proving the occurrence of various types of ion-pairs in solvolytic reactions, proposed by Goering[229], consisted in simultaneous study of rates of randomisation (equilibration), racemisation, and solvolysis of labelled (at carbonyl or ethereal oxygen atoms) optically active alkyl *p*-nitrobenzoates, e.g.[209]



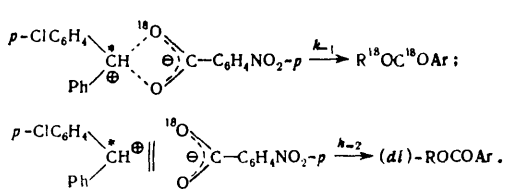
Analysis of the initial compound at various degrees of conversion revealed "scrambling" (equilibration) of the tracer in the returned product and loss of stereochemical configuration; however, these processes take place at different rates:

$$ROCOAr \xrightarrow{k_t} ROH + ArCOOH; \quad (1)$$

$$ROC^{18}OAr \xrightarrow{k_{eq}} R^{18}OC^{18}OAr; \quad (2)$$

$$(d \text{ or } l)\text{-}ROCOAr \xrightarrow{k_{rac}} d, l\text{-}ROCOAr. \quad (3)$$

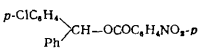
Thus for *p*-chlorodiphenylethyl *p*-nitrobenzoate in 80% and 90% aqueous acetone the rate of randomisation exceeds the rate of the solvolytic reaction ($k_{eq} > k_t$). The fact that k_t does not coincide with k_{eq} and k_{rac} implies that processes (2) and (3) result not only from the return of ions to the original covalent compound but also from the return of other ionic intermediates, as the difference between k_{eq} and k_{rac} indicates the existence of at least two such ionic intermediates. Usually $k_{eq} > k_{rac}$: e.g. for the system under discussion their ratio is 1.5 and 2.5 in 80% and 90% acetone respectively. This suggests that equilibration of the label has already occurred at the stage of return of the contact ion-pair, but racemisation on return of a solvate-separated ion-pair (the anionic component "slides" over the surface of the cation), while the solvolytic reaction involves solvate-separated ion-pairs and free ions:



The results show that in 90% acetone 72% of the ion-pairs formed are converted back into the original covalent compound, and 81% of the return occurs with retention of configuration. The rate constant k_{eq} may not represent the total return of ion-pairs (on the assumption that part takes place without randomisation) but be its lower limit.

Proof that return of an internal ion-pair may occur with complete retention of stereochemical configuration and proof of the existence of various types of ion-pairs were obtained in a study of the effects of additions of sodium azide on k_t, k_{eq}, and k_{rac}.[210] The presence of this additive was found to increase the rate of solvolysis, somewhat to diminish the rate of randomisation, and completely to suppress racemisation of the initial compound.

Table 7. Values of k_t, k_{eq}, and k_{rac} in the hydrolysis of *p*-chlorodiphenylethyl *p*-nitrobenzoate in 80% acetone at 99.0°C, in the presence and in the absence of sodium azide



(80% acetone with $c_0 \simeq 0.028$ M at 99.6°C).

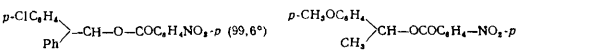
10^3k, h^{-1}	NaN_3 absent	0.14 M NaN_3
k_t	4.41	30.0
k_{eq}	6.5	5.9
k_{rac}	2.76	0.0

These results are consistent with the view that sodium azide is a nucleophilic "trap" for external ion-pairs. Exchange of anions between the ion-pairs

$$R^+\|X^- + Na^+\|N_3^- \rightleftharpoons R^+\|N_3^- + Na^+\|X^-$$

produces a more reactive ion-pair, which almost completely suppresses return from the solvent-separated ion-pair. Hence loss of stereochemical configuration is a consequence of return of this particular ion-pair (Table 7). Some change in k_{eq} under the influence of sodium azide implies that part of the randomisation is due to the return of loose ion-pairs. The fractional return increases with increase in the stability of the ion-pair. Thus k_t = 0.0064 h^{-1} and k_{eq} = 0.0187 h^{-1} even for diphenylethyl *p*-nitrobenzoate in 90% acetone (at 118.6°C).

Table 8. Effect of water content of acetone on proportion and stereochemistry of return for



Acetone	90%	80%	90%	70%
k_t (rel.)	1	9	1	45
k_{eq}/k_t	2.1	1.46	2.59	0.57
k_{rac}/k_{eq}	0.38	0.43	0.45	0.71

Increasing the water content in aqueous acetone affects both the fractional return (k_{eq}/k_t) and the stereochemistry of return (k_{rac}/k_{eq}).[230] The rates of solvolysis of

p-chlorodiphenylethyl and 1-*p*-methoxyphenylethyl *p*-nitrobenzoates increase, while the ratio k_{eq}/k_t decreases (for the latter compound in 70% acetone it even becomes <1) and k_{rac}/k_{eq} increases (Table 8). This observation is fully consistent with the above hypothetical shift in equilibrium, in a more strongly ionising medium, from contact to loose ion-pairs.

The fractional return from a solvate-separated ion-pair depends on its stability. A more stable ionic intermediate is in general less susceptible to nucleophilic attack, and is therefore more strongly racemised. Another possible explanation is that the forces of interaction between the ionic components become weaker in such an ion-pair, which increases the fractional return with racemisation. This may be illustrated by comparing results obtained for the solvolysis of 1-phenylethyl *p*-nitrobenzoate in 70% acetone, when no appreciable racemisation was observed, and for that of the 1-*p*-methoxyphenylethyl ester, which was more reactive by a factor of ~30 000, and 71% return occurred with racemisation [230]. Thus increase in the stability of $R^+\|X^-$ leads to increases both in the ionisation constant and in the fractional return k_N/k_S (the ratio of the rate constants for reaction with its own gegenion and for reaction of the ion-pair with the solvent).

Winstein et al. [162] noted an increased contribution by return of the solvent-separated pair accompanied by increase in the rate of solvolysis in acetic acid on passing from 1-phenylethyl to 1-*p*-methoxyphenylethyl toluene-*p*-sulphonate, as shown by the increase in the salt effect from normal to special ($k^0_{ext}/k^0_t = 1$ and 3.2 respectively). A similar relationship was observed for *para*-substituted diphenylethyl *p*-nitrobenzoates [231]: k_t increased rapidly in the sequence Cl < H < CH_3 < CH_3O ($\rho = -3.9$ in agreement with an S_N1 mechanism), while k_{eq}/k_t showed little change, and k_{rac}/k_{eq} increased with k_t, i.e. with increase in stability of the ionic intermediate.

The species through which return takes place to the original compound is recognised from the common-ion effect, the salt effect, and the rate constants k_{eq} and k_{rac}. Thus it was deduced from the absence of depression by a common ion that with 1-*p*-methoxyphenylethyl toluene-*p*-sulphonate return occurs only from solvent-separated ion-pairs, whereas free ions are also involved in the case of the 1-(2,4-dimethoxyphenyl)ethyl ester [188]. The special salt effect and the greater selectivity observed in the solvolysis of *threo*-*p*-methoxy-$\alpha\beta$-dimethylphenethyl toluene-*p*-sulphonate in comparison with the $\alpha\beta$-dimethylphenethyl ester correspond also to the nature of the ion-pairs involved in return: in the former case solvolysis is accompanied by the return of 83% of loose and 38% of contact ion-pairs; whereas in the latter case return takes place only from contact ion-pairs, although the total amount of return (78%) is the same in the two cases [188]. Passing from 2-phenylpropyl to 2-*p*-methoxyphenylpropyl toluene-*p*-sulphonate is also accompanied by an increase in the fractional return from loose ion-pairs [232].

A more complex question is the effect of additions of sodium azide on the ratios k_{eq}/k_t and k_{rac}/k_{eq}. Thus, in contrast to the above reaction of *p*-chlorodiphenylethyl *p*-dinitrobenzoate, the addition of sodium or tetrabutylammonium azide in the reactions of 1-*p*-methoxyphenylethyl [230] and phenyl-*p*-tolylmethyl [231] *p*-nitrobenzoates leads not only to an increase in k_t but also to a considerable decrease in the fractional return (k_{eq}/k_t), though the stereochemistry of return (k_{rac}/k_{eq}) remains almost unchanged, for which no simple explanation is available. It may be linked [230,231] with a diminution in the forces of interaction in the contact ion-pair (resulting from increased delocalisation of charge in the cationic component), so that racemisations may already occur on return of the contact ion-pair.

Redistribution of the label in the anionic component was used by Winstein et al. [233] to prove the presence of ion-pairs in the reactions of non-activated secondary alkyl sulphonates, such as 1-methylheptyl and *trans*-4-t-butylcyclohexyl toluene-*p*-sulphonates, for which bimolecular attack on the contact ion-pair is assumed in conformity with Sneen's mechanism [183]. Randomisation was demonstrated, and k_{eq} was unaffected by addition of the same anion. The proportion of this process

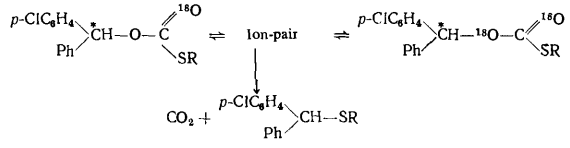
$$ROS^{18}O_2Ar \underset{}{\overset{k_{eq}}{\rightleftharpoons}} R^{18}OS^{18}O_2Ar$$

increases as the solvent becomes less strongly nucleophilic (Table 9).

Table 9.

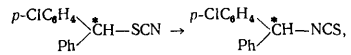
Solvent	MeOH	AcOH	HCOOH	CF_3COOH
$\frac{k_{eq}}{k_{eq}+k_t}$	1.1 (75°)	6.5 (75°)	8.1(25°)	19.9 (25°)

Equilibration of the label and loss of optical activity in the initial compound have been observed in the decomposition of *p*-chlorodiphenylmethyl *S*-alkyl(or aryl) thiocarbonates in various solvents [234] (S_Ni mechanism), with the ratio of the constants depending on the nature of the solvent. The results indicate that return of the ion-pairs took place predominantly with retention of configuration ($k_{eq} > k_\alpha$): [235]



In the corresponding reaction of $RCH(CH_3)OCOCl$ in dioxan, however, no exchange of the tracer between ethereal and carbonyl oxygen atoms was observed [236]. The above results on equilibration of the oxygen label in the carboxylate and other anions show that this process occurs mainly at the stage of return of internal ion-pairs.

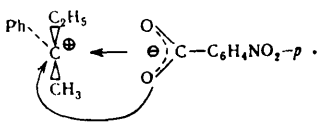
Similar results were obtained for isomerisation in a system containing thiocyanate, another ambident anion. Optically active *p*-chlorodiphenylmethyl thiocyanate underwent isomerisation in various solvents with complete retention of configuration [236–240]:



i.e. most probably as a result of return of a contact ion-pair.

Thus considerable return was usually observed with secondary alkyl *p*-nitrobenzoates ($k_{eq}/k_t = 2.2-3.2$ for 90% acetone), and a substantial proportion of the return (38–53% depending on structure) involved racemisation, but different rules were obtained for tertiary alkyl systems. In the reaction of α-ethyl-α-methylbenzyl-*p*-nitrobenzoate

$k_{eq} < k_t$ ($k_{eq}/k_t = 0.6$),[241] although both constants increased on passing to the tertiary alkyl, and only 8% of the return involved racemisation. The reason for the diminished return is not clear, although it may be linked with greater instability of a tertiary than of a secondary ion-pair due to an enhanced tendency to dissociation. The greater stereospecificity of return was attributed[242] to a heightened barrier to rotation of the anion around the sterically hindered cation



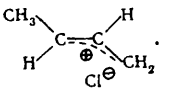
Fundamentally, however, the situation was unchanged: solvolytic reactions of tertiary systems involve ion-pairs capable of conversion into the original compound.

Return, as indicated by randomisation, was observed with triphenylmethyl *p*-nitrobenzoate dissolved in anhydrous acetone[242], i.e. in the absence of reaction. However, contradictory results were obtained for the effect of the azide ion[242-244]. According to Swain et al.[242] lithium azide converts the whole of the ester into triphenylmethyl azide and completely inhibits return (k_{eq} falls to zero), from which it was concluded that rearrangement took place in the intermediate that was captured by the azide ion. According to Winstein et al.[243], however, tetrabutylammonium azide does not suppress return, although in 99.2% acetone its addition, without changing the overall rate of the process, completely suppressed solvolysis: i.e. then $k_t = k_{N_3^-}$. In contrast to the quaternary ammonium azide, the lithium salt greatly diminishes return and sharply increases $k_t = k_{N_3^-}$. Since lithium perchlorate exerts an unusually marked influence on the rate of ionisation, it is supposed that in aprotic media lithium salts are able to form quadrupoles with ion-pairs, thereby promoting ionisation.

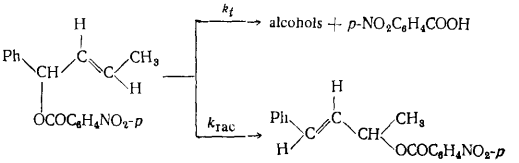
5. Isomerisation in Allyl Systems

Evidence of the occurrence of ion-pairs in solvolytic reactions and of a return mechanism is provided by isomerisation of the allyl fragment during the reaction of unsymmetrically substituted allyl systems, which have been studied in very great detail[245-253]. The intramolecular character of the isomerisation must first be demonstrated before the presence of ion-pairs can be assumed in these reactions. The actual idea of the existence of ionic intermediates other than free carbonium ions, through which both solvolysis and intramolecular rearrangements can be effected, was first put forward[7] in a study precisely of the allyl rearrangement: acetolysis of 1,1-dimethylallyl chloride was shown to be accompanied by its rearrangement into 3,3-dimethylallyl chloride, the rate of rearrangement being unchanged (allowing for the salt effect) when the reaction was conducted in the presence of the chloride ion. On the addition of $*Cl^-$ only a small proportion of the label entered the initial compound[25].

Thus the observed isomerisation is due to return of an ion-pair. The action of aqueous silver nitrate on *cis*- and *trans*-but-2-enyl and 1-methylallyl chlorides gives mixtures of isomers (nitrates and alcohols) with retention of geometrical configuration, which was attributed to a fairly high barrier opposing rotation in the ionic intermediate[245]

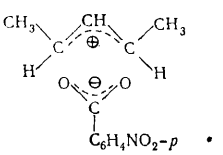


Solvolysis of 1-phenylbut-2-enyl *p*-nitrobenzoate in aqueous acetone[246,247], dioxan, and methanol[248,249] is accompanied by its intramolecular isomerisation into the less reactive α-methylcinnamyl ester:

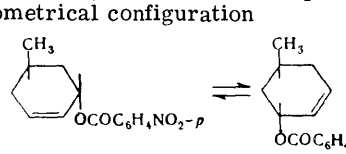


Use of the labelled optically active ester showed[247] that, in 90% aqueous acetone at 99.4°C, the relative rate constants (in 10^2 h^{-1}) were $k_t : k_{rac} : k_{eq} = 5.16 : 7.04 : 10.88$: i.e. under these conditions 65% of the return was accompanied by loss of stereochemical configuration. As noted earlier, the fractional return, i.e. the ratio k_{eq}/k_t, diminished with increase in the water content of the acetone, but, in contrast to other alkyl benzoates, the fractional return with racemisation k_{rac}/k_{eq} also decreased (to 16% in 70% acetone at 49.04°C).

The solvolysis of optically active *trans*-1-methylbut-2-enyl *p*-nitrobenzoate in aqueous acetone also was accompanied by randomisation and racemisation of the starting material, since the rate of loss of optical activity $k_\alpha = k_t + k_{rac}$ exceeded considerably the rate of solvolysis ($k_\alpha/k_t = 5.4$ and 2.17 in 90% acetone at 99.6°C and in 60% acetone at 59.9°C respectively)[250,251], so that by the time of 50% reaction the initial ester has been 95% racemised. The intramolecular character of the isomerisation (racemisation) was proved by the absence of exchange between the anions and *p*-nitrobenzoic acid and by the lack of effect of salt additions on k_t and k_α. It it interesting that $k_{eq} = k_{rac}$ (in 80% and 60% acetone): i.e. the two processes take place via the same symmetrical ion-pair (probably a contact pair, since exchange is absent), in which the two oxygen atoms and the two allyl carbon atoms are equivalent (cationic and anionic components are assumed to be located in perpendicular planes)



A similar relation was observed in the solvolysis of *cis*-5-methylcyclohex-2-enyl *p*-nitrobenzoate[252]. In the allyl isomerisation of the optically active *trans*-ester in 80% acetone, however, which also takes place with retention of the geometrical configuration



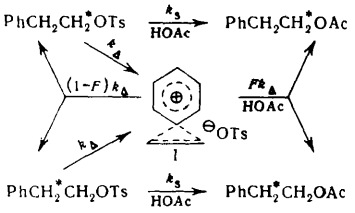
the rate of randomisation is double the rate of racemisation[253]. This system thus presents a more general situation, with two intermediates present in equilibrium: one is common to the two enantiomers, and its return leads both to racemisation and to randomisation; the other is not common, and only equilibration without loss of stereochemical configuration takes place in it (i.e. return occurs

without change in the carbon reaction centre). However, the reason for the differing behaviour of the two geometrical isomers is obscure.

6. Rearrangements with Aryl Participation

The concept of ion-pairs proved necessary to explain results connected with aryl migration and the stereochemistry of solvolysis in systems containing a 2-arylethyl fragment. From the very first steps in investigating the problem of "non-classical" (bridging) carbonium ions and anchimeric assistance it was demonstrated that this problem is closely connected with that of the formation of ion-pairs in these reactions [186,254].

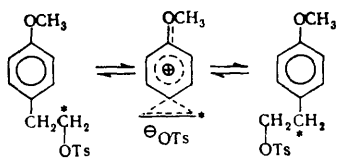
If migration of an aryl group during solvolysis in such systems is intramolecular, i.e. if it is independent of addition of a common ion, investigation of the rate of migration can be used to determine the fractional return from ion-pairs ("non-classical") formed with anchimeric assistance (k_Δ). Occurrence of a migration process can be assessed by using an unsymmetrically substituted system or, most simply, by examining the distribution of an isotropic tracer in a (carbon or hydrogen) labelled symmetrical system:



$$k_t = k_s + Fk_\Delta$$

The acetolysis rate constants for phenethyl toluene-p-sulphonate at 90°C are [255] $k_S = 8.92 \times 10^{-7}$ s^{-1} and $k_\Delta = 1.18 \times 10^{-6}$ s^{-1}, while the ion-pair return rate constant is 8.00×10^{-7} s^{-1}, which is comparable with k_S.

Many papers have appeared [255-270,273] on the effect of the aryl group and the medium on the distribution of a radioactive label in the initial compound, with calculations of the proportions of the process occurring with and without anchimeric assistance (k_Δ and k_S). Unfortunately, the nature of the ionic intermediate from which return occurred was not always studied. Return may involve not only ion-pairs but also free ions depending on structure and solvent, and these processes may occur together [271]. In some cases, however, the intramolecular character of return has been proved [255]. Thus solvolysis of carbon-labelled p-methoxyphenethyl toluene-p-sulphonate results in dissemination of the tracer both in the solvolysis product and in the initial ester [258], the latter process being a consequence of intramolecular rearrangement:



The intramolecular character of the rearrangement has been shown also in the acetolysis of β-methylphenethyl p-bromobenzenesulphonate [272] and p-methoxy-2-methylphenethyl toluene-p-sulphonate [232]. Hence participation of ion-pairs is possible even in the reactions of primary alkyl systems, providing that the substrate contains groups capable of assisting ionisation.

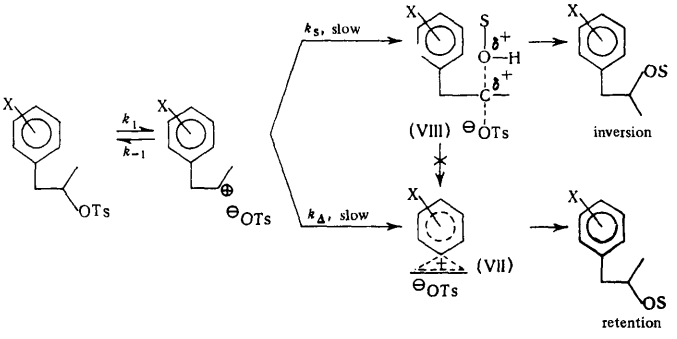
Results for the trifluoroacetolysis of phenethyl toluene-p-sulphonate [271], in which the path with anchimeric assistance is greatly enhanced, ($k_\Delta/k_S = 23\,000$), can be explained only if all three types of ion-pairs are involved in the process. Their contributions to the total return are indicated by the scheme

$$\mathrm{ROTs} \underset{15\%}{\rightleftharpoons} \mathrm{R^{\oplus}OTs^{\ominus}} \underset{87\%}{\overset{85\%}{\rightleftharpoons}} \underset{\text{Product}}{\mathrm{R^{\ominus}\,\|\,{}^{\ominus}OTs}} \overset{11.8\%}{\rightleftharpoons} \underset{\text{Product}}{\mathrm{R^{\ominus}}} + {}^{\ominus}\mathrm{OTs}\ .$$

Similarly for the p-methoxyphenethyl ester [258,271]

$$\mathrm{ROTs} \underset{8\%}{\rightleftharpoons} \mathrm{R^{\oplus}OTs^{\ominus}} \underset{95\%}{\overset{92\%}{\rightleftharpoons}} \underset{\text{Product}}{\mathrm{R^{\oplus}\,\|\,{}^{\ominus}OTs}} \overset{2.5\%}{\rightleftharpoons} \underset{\text{Product}}{\mathrm{R^{\oplus}}} + {}^{\ominus}\mathrm{OTs}\ .$$

Thus systems with a bridging capability undergo solvolysis in two ways—attack by the solvent on the substrate and attack by the aryl group on the carbonium centre—corresponding to the rate constants k_S and k_Δ. In the case of secondary substrates the first process gives a product with inversion of configuration [272]. The present Review will not discuss the mechanism of stabilisation of the carbonium centre by neighbouring groups, nor methods of resolving the observed constant k_t into k_S and k_Δ (we mention merely that this is effected both from the percentage rearrangement and the stereochemistry and from a correlation analysis [274,275]). Nor shall we consider the controversial question [276,277] of the existence of two rapidly rearranging classical ion-pairs instead of a "non-classical" ion-pair. The fundamental question here will be the presence of a stage of intramolecular return, indicating that structure (VII) is an intermediate, not the transition state of the dissociation stage.



An important aspect of the reaction mechanism, especially in secondary systems, is possible participation by ion-pairs even at a stage not involving anchimeric assistance. In these systems both processes (attack by the solvent and by the aryl group) may be supposed to involve not the covalent compound but an intimate ion-pair formed in a pre-equilibrium stage [277]. It is possible also that an ion-pair differing from (VII) (e.g. a nucleophilically solvated ion-pair) may be formed along the k_S path, from which return may occur also (this is important, since return from (VII) diminishes the anchimerically assisted proportion of the process). It is important only to remember that the k_S and k_Δ paths do not intersect [255]: i.e. the ion-pairs formed (VIII) are unable (e.g. because solvation prevents aryl attack) to pass into (VII) (otherwise it would have been impossible to explain the good agreement between kinetic results and analyses of the products).

However, a test for the reaction mechanism shows the possibility of direct S_N2 attack by the azide ion on the covalent compound in primary and secondary systems [270,278].

Table 10.

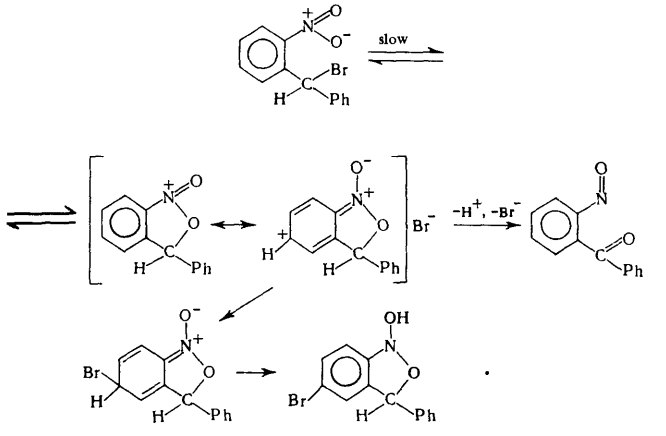
	CF_3COOH	HCOOH	AcOH
erythro-	92	61	29
threo-	89	49	22

Although proofs of the existence of ion-pairs have been obtained mainly in connection with aryl-group participation, k_Δ processes involving other β-donor groups may reasonably be expected to occur similarly. An example is the rearrangement of *erythro*- and *threo*-isomers of 4-chloro-1-methylpentyl toluene-*p*-sulphonate [279], in which considerable retention of configuration was observed. Table 10 shows that the fractional retention increases with increase in the ionising power of the solvent and decrease in its nucleophilicity. The concept of ion-pairs is especially reasonable for explaining rearrangements in primary systems, where the formation of free carbonium ions is unlikely.

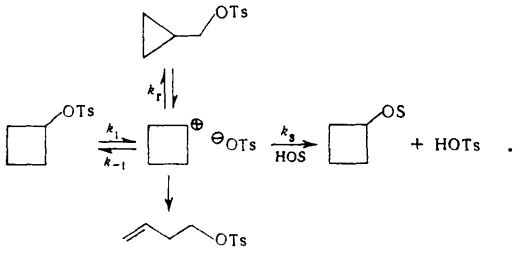
7. Other Cases of Isomerisation of the Cationic Component

Besides the above cases of allyl rearrangement and migration of an aryl group, other examples are known of rearrangements in the cationic component, which also are easily explained by the formation of ionic intermediates.

The nature of the product is changed by a curious isomerisation discovered recently [280]. In the solvolysis of *o*-nitrodiphenylmethyl bromide in 90% aqueous acetone, acidification with aqueous hydrobromic acid yields 5-bromo-3-phenyl-1-2,1-benzisoxazole instead of *o*-nitrosobenzophenone, which is the reaction product in neutral solution. The two reactions are assumed to occur via the same ion-pair formed by intramolecular attack by the nitro-group. Abstraction of a proton from this ion-pair (by the action of water or of added sodium acetate) yields the ketone, and reversible return of the pair in acid medium is accompanied by entry of bromine into the ring to give a product converted into the isoxazole derivative:



The formation of ion-pairs (probably of contact type) explains the isomerisation observed in the solvolysis of cyclopropylmethyl [281] and cyclobutyl [179,282] arenesulphonates:



It has been shown above, on the basis of the effect of the leaving group and data on competing reactions, that free ions are not formed, and the ratio k_r/k_S depends on the nature of the leaving group [179], as should be the case in reactions involving an ion-pair.

VI. CONTACT ION-PAIRS IN S_N2 REACTIONS

The concept of ion-pairs has thus provided explanations of the relations among rates of solvolysis, racemisation, randomisation, and rearrangement, as well as the special salt effect, in solvolytic reactions of type S_N1. Formation of ionic intermediate has recently been considered also in S_N2 reactions of secondary alkyl systems. Since 1965 the possibility has been discussed that bimolecular nucleophilic substitution may result from nucleophilic attack not on the covalent compound but on a contact ion-pair formed in the pre-equilibrium stage:

$$RX \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^+X^- \xrightarrow[\text{slow}]{N^-,k_2} RN + X^- .$$

Since secondary compounds should be less reactive than primary compounds by an S_N2 mechanism, and less reactive than tertiary compounds by an S_N1 mechanism, Sneen supposed [183,283-294] that the nucleophile may be attacking a contact ion-pair. He based this suggestion on two facts—(i) formation of the completely inverted alcohol on the hydrolysis of optically active 1-methylheptyl methanesulphonate [283] and (ii) the non-coincidence of the rate-determining stage and the stage governing the ratio of the products (alcohol and azide) of the solvolysis of this compound in the presence of sodium azide in 25% and 30% aqueous dioxan [284].

In the classic S_N1 mechanism the reaction velocity is indeed unaffected by addition of sodium azide, since attack occurs after the rate-determining stage. Addition of the azide ion may than serve as a test for the S_N1 character of a solvolytic process [87], since, if reaction does not occur by an S_N2 mechanism even with a strong nucleophile, this should apply even more to a weaker nucleophile (water, alcohols). In the classic S_N2 mechanism the rate should increase in proportion to the increase in concentration of sodium azide:

$$RX \begin{cases} \xrightarrow{k_S} ROS \\ \xrightarrow{k_N\cdot[N_3^-]} RN_3 \end{cases} ; \quad k_{obs} = k_S + k_N[N_3^-] .$$

An intermediate case was observed with s-octyl sulphonates: the rate of reaction measured by the consumption of the initial compound increases with the sodium azide concentration, but considerably less rapidly than in

an S_N2 process (the order with respect to the azide ion lies between zero and unity). However, the selectivity with respect to the azide ion is about a thousandfold that for an S_N1 reaction. Thus addition of the azide ion provided Sneen and his coworkers with a convincing argument that an S_N2 reaction results from attack by the nucleophile on a contact ion-pair, which explained both the stereochemical inversion, the kinetic data, and the distribution of the products. Application of the steady-state principle to the scheme

$$RX \underset{\text{rapid}}{\rightleftharpoons} R^+X^- \begin{cases} \xrightarrow[\text{slow}]{k_S} ROS \\ \xrightarrow{k_N} RN_3 \end{cases}$$

yields the equation

$$k_{obs} = \frac{k_1 (k_S + k_N \cdot [N_3^-])}{k_{-1} + k_S + k_N \cdot [N_3^-]},$$

showing that k_{obs} is a complicated function of k_1, k_{-1}, k_S, and k_N. The ratio k_N/k_S is determined from the proportions of products formed in the presence of various concentrations of sodium azide:

$$\frac{k_N [N_3^-]}{k_S} = \frac{[RN_3]}{[ROH]}.$$

This approach removes objections based on the variation of the reactivity of sodium azide with concentration. Of course, F_N can be determined from the plot of $[RN_3]/[ROH]$ against $[N_3^-]$ if the latter is a straight line. However, the dependence would not be linear over a wide concentration range, since sodium azide may be incompletely dissociated in these solutions. Indeed, according to Ritchie [145] the graph for the reaction of di-*p*-methoxyphenylmethyl 2,4,6-trimethylbenzoate in methanol is not linear. The observed fractional order with respect to the azide ion may then be a consequence of its incomplete dissociation. However, this aspect has not been discussed in the publications of Sneen and his collaborators. It is noteworthy that departures from the first order with respect to the bromide ion, observed in a study of the rate of racemisation of 1-phenylethyl bromide in acetone, were due to the existence of lithium bromide in this solvent not only as ions but also as ion-pairs [33], although they could easily have been attributed to an ion-pair S_N2 mechanism.

The ratio of the observed rate constant to the solvolytic rate constant k_{NA} in the absence of sodium azide, allowing for a possible slight positive salt effect (assumed to correspond to that produced by salts such as lithium perchlorate, sodium nitrate, and sodium bromide), is given by

$$\frac{k_{obs}}{k_{NA}} = \frac{(x+1)(1+m[N_3^-])}{(x+1+m[N_3^-])}$$

$$m = \frac{k_N}{k_S}, \quad x = \frac{k_{-1}}{k_S}$$

$$k_{NA} = k_{NA}^0 (1 + b \cdot [NaN_3]).$$

The S_N2 and S_N1 mechanisms are extreme cases of this equation (as $x \to \infty$ and 0 respectively). The variation of k_{obs}/k_{NA} at intermediate values of x is represented by curve *1* in Fig. 3. The experimental constant for 1-methylheptyl methanesulphonate coincides with the value calculated for 25% and 30% dioxan with $x = 2.4$ and and 2.59 on the assumption that $b = 1.08$ and 1.04 respectively [287]. However, Schleyer et al. [295] have shown that observed rate constants obtained at different concentrations can be described by the equation for an S_N2 reaction (i.e. they can be correlated with the distribution of products) on the assumption that sodium azide exerts a negative salt effect ($b = -0.3$ and -1.0 for 25% and 30% dioxan respectively). The dependence of the ratio k_{obs}/k_{NA} on the sodium azide concentration will then be linear, in conformity with an S_N2 mechanism. However, values of b for closely similar media may then differ very greatly. Furthermore, Schleyer et al. [295] showed that the reaction of 1-methylheptyl *p*-bromobenzenesulphonate and of isopropyl toluene-*p*-sulphonate with the azide ion in 80% aqueous ethanol is the usual S_N2 type of process, in which the rate-determining stage coincides with the stage determining the composition of the products.

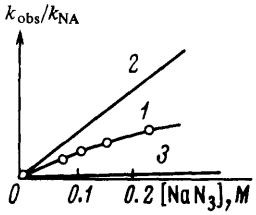
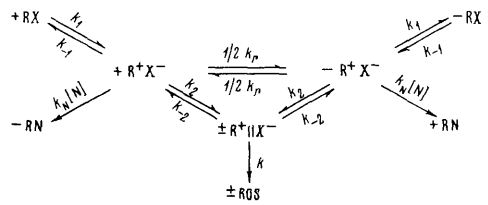


Figure 3. Dependence of k_{obs}/k_{NA} on $[NaN_3]$ for the reaction of 1-methylheptyl methanesulphonate with the azide ion and with water in 25% aqueous dioxan based on experimental value of $k_N/k_S = 8.22$ and different values of x: 1) 2.40; 2) ∞ (S_N2 mechanism); 3) 0 (S_N1).

The above procedure was applied by Sneen et al. to various systems, e.g. the reaction of *p*-methoxybenzyl chloride with water and the azide ion in 70% aqueous dioxan and that of benzoyl chloride with *o*-nitroaniline and water in 50% aqueous acetone [288]. On the assumption of a positive salt effect calculated and observed ratios k_{obs}/k_{NA} can be reconciled with $x = 1.98$ and 1.1 respectively ($m = 21.6$ and 4.42 from experiment).

An S_N2 mechanism with nucleophilic attack on a contact ion-pair has been suggested by Sneen et al. for the reactions of 1-arylethyl halides in ethanol [289] and of sulphonium salts [290]. The proposed scheme explains also results obtained in allyl systems [292–294]. In the solvolysis of 1-methylbut-2-enyl chloride in the presence of azide or thiocyanate ions in absolute ethanol $x = k_{-1}/k_S = 4.0$ for both ions [291]. This was regarded as supporting the scheme, which can in general be written



where k_r is the allyl isomerisation rate constant.

A similar view was expressed by Streitwieser et al. [296], who showed [297] that acetolysis of 1-methylheptyl toluene-*p*-sulphonate entails inversion but is accompanied by racemisation of the initial compound, the rate of which is

increased by the presence of lithium toluene-*p*-sulphonate [296]. According to Streitwieser solvolysis and substitution are not independent processes, but occur via the same ionic intermediate, together with slight rearrangement

$$ROTs \rightleftharpoons R^+OTs^- \rightleftharpoons R'^+OTs^- \rightleftharpoons R'OTs$$
$$\searrow \quad \swarrow$$
$$\text{Solvolysis products}$$

The observed effect of additions of lithium perchlorate on the rates of solvolysis, racemisation, and rearrangement were attributed to "capture" of the ion-pair, similar to that effected by the azide ion. Thus in the reactions of non-activated secondary systems, in contrast to Winstein's description of S_N1 processes, all events (anion exchange, return, solvolysis) involve contact ion-pairs, which in Winstein's scheme played no part in chemical "capture". It is significant also that the limiting stage is not the formation of these ion-pairs but their further transformation. The reason for these differences is that nucleophilic attack on a secondary ion-pair is more favoured than is its further ionisation and dissociation.

When the various secondary systems for which Winstein's scheme was used are recalled, many questions arise, to which it is difficult to give an unequivocal answer. It must be admitted, for example, that all processes involving solvent-separated ion-pairs formed in the limiting stage should be more rapid than any process described by an ion-pair S_N2 mechanism, otherwise it would be impossible to explain why they did not result from attack on a contact ion-pair. Unfortunately, no comparison was made of the rates of various processes under identical conditions.

It was shown in the same year (1965) that the reaction of 1-methylheptyl bromide with silver nitrate in acetonitrile, with formation of an alkene and an alkyl nitrate, entails inversion of the stereochemical configuration (the optical purity of the alkyl nitrate was 87%) [298]. A similar rule was observed in the reaction of the bromide with silver perchlorate in benzene: formation of the alkyl perchlorate was 80% accompanied by inversion of configuration [299]. The slow stage was considered to be attack by the nucleophile on the complex $RX\ldots Ag^+$, and a quadrupole $[N^-\ldots R^+\ldots X^-\ldots Ag^+]$ was assumed, in the traditions of the English school, to be involved in the reaction. Such a structure had been suggested earlier as a transition state [300]. The reactions of alkyl halides with silver nitrate or silver perchlorate in acetonitrile had the same mechanism (not S_N1Ag^+ [1]). [301] However, it is easily seen that the differences from Sneen's treatment are mainly terminological [302,303].

In view of the possibility that ion-pairs of contact type may take part in nucleophilic substitution Winstein's scheme should be expanded, and should include in modified form the various mechanisms that can in principle operate with variation in the relative rates of the different stages:

$$\begin{array}{ccccccc}
 & S_N^I1 & & S_N^{II}1 & & S_N^{III}1 & \\
 & k_1 & & k_2 & & k_3 & \\
RX & \rightleftharpoons & R^+X^- & \rightleftharpoons & R^+\,\|\,X^- & \rightleftharpoons & R^+ + X^- \\
\text{(I)} & k_{-1} & \text{(II)} & k_{-2} & \text{(III)} & k_{-3} & \text{(IV)} \\
S_N^I2 \downarrow & k_S & S_N^{II}2 \downarrow & k_S^{II} & S_N^{III}2 \downarrow & k_S^{III} & S_N^{IV}2 \downarrow \; k_S^{IV} \\
\text{ROS} & & \text{ROS} & & \text{ROS} & & \text{ROS}
\end{array}$$

Participation of ion-pairs in reactions of secondary systems, including Sneen's ion-pair mechanism ($S_N^{II}2$), follows from the efforts by Shiner et al. [304-310] to determine the mechanism of solvolytic reactions from α- and β-deuterium isotope effects. For example, the α-effect in the reactions of isopropyl *p*-bromobenzenesulphonate [305], 1-methylbut-2-enyl derivatives [306], cyclopentyl *p*-bromobenzenesulphonate [310], etc. is close to unity in aqueous ethanol, but increases to 1.22–1.23 as the ionising power of the solvent increases and its nucleophilicity diminishes (ethanol with a high water content, aqueous trifluoroethanol, carboxylic acids). This was regarded as evidence of a change in mechanism from "purely" S_N2 to S_N^I1 or $S_N^{II}2$, in the limit $S_N^{II}1$; the classification is based on a scheme which differentiates between the mechanisms of the formation of a contact ion-pair in the limiting stage (S_N^I1) and of its conversion into a solvent-separated ion-pair ($S_N^{II}1$). α-Deuterium effects of 1.00–1.05, ~1.15, and 1.22 are regarded as representing S_N^I2, S_N^I1 or $S_N^{II}2$, and $S_N^{II}1$ mechanisms respectively (the last indicates conversion of a contact into a solvent-separated ion-pair). A large isotope effect is associated with formation of a carbonium ion [311]. However, the presence of a certain effect of the azide ion on the rate of reaction of secondary systems would probably indicate $S_N^{II}2$, not an S_N^I1 mechanism.

Nevertheless, it seems to the Reviewer premature to regard the criterion proposed by Shiner and his coworkers as absolutely reliable, and to try to identify reaction mechanisms on the basis of relatively small (1.08–1.22) α-deuterium isotope effects. Other grounds also exist for a cautious attitude to this criterion. Thus the observed isotope effect develops differently at different stages [312], and would depend on the relative rates of conversion of the ion-pair and of the return stage, since

$$\frac{k_2^D}{k_{-1}^D} \Big/ \frac{k_2^H}{k_{-1}^H} \neq 1.$$

Furthermore, this approach does not apply to reactions in which elimination and rearrangement occur as well as substitution [313], and such competing processes usually accompany reactions in secondary systems [314]. Finally, the maximum isotope effect was assigned to an $S_N^{II}1$ reaction on the basis of results [305] that have since proved incorrect [315].

Bordwell et al. [316-319] give arguments supporting the involvement of ion-pairs in S_N2 nucleophilic substitution at a tertiary carbon atom in the allylic systems

$$p\text{-}MeC_6H_4SO_2 \diagdown \quad H \diagup C{=}C \diagdown \quad H \diagup C(Me_2)X \xrightarrow[\text{MeOH or DMF}]{N^-} RN$$

in which X = Cl, Br, OSO_2CH_3; N = OCH_3, OH, N_3, SCN, $S{:}C(NH_2)_2$. With the first order with respect to the nucleophile (which corresponds to an S_N1 mechanism) the dependence of reaction velocity on salt effect, polarity of medium, nature of nucleophile, leaving group, and the β-deuterium effect is different from that found for a system having a primary carbon atom. Introduction of an arenesulphonyl group is assumed to inhibit the dissociation but not the formation of ion-pairs.

Sneen's mechanism has recently been supported [320] by examination of the kinetic chlorine isotope effect $^{35}k/^{37}k$ in the reaction of *p*-methoxybenzyl chloride with sodium azide in 70% aqueous acetone. The isotope effect varied with the nucleophile concentration, which should not occur [320] in S_N1 and S_N2 processes, but is consistent with an ion-pair S_N2 mechanism.

An attempt was made to transfer Sneen's mechanism to reactions of non-activated primary systems [321,322]. It had earlier been suggested, in the reactions of AlkX with silver salts AgY (where Y = NO_3^-, $OSO_2C_6H_4CH_3$, etc.), that an ion pair Y^-R^+ is formed in the slow stage [323,324], and recombines or forms an alkene in the rapid stage. Scott [321] concluded that reactivity and selectivity data for methyl halides with various nucleophiles in water were best explained by the involvement of contact ion-pairs in the slow stage (i.e. that $k_{obs} = K_{eq} k_2$). However, such a hypothesis gives rise to grave objections [325]. Abraham's calculation [326] of the free energy required to form a primary ion-pair in water makes the hypothesis improbable, although ion-pairs may be formed with isopropyl and t-butyl bromides. Furthermore, the α-deuterium isotope effect in primary systems is close to unity [313].

Kohnstam and his coworkers [327,328] disputed the involvement of contact ion-pairs in the S_N2 mechanism and opposed attempts to establish a "unified" mechanism of nucleophilic substitution. In their view the influence of sodium azide on the hydrolysis of s-octyl methanesulphonates could be described, within the framework of the classic mechanisms, as occurring in a boundary region in which reaction took place simultaneously by S_N1 and S_N2 mechanisms§. These workers showed [328] that the hydrolysis of *para*-substituted (methoxylated and phenoxylated) benzyl chlorides and diphenylmethyl chloride takes place by an S_N1 mechanism, and that addition of sodium azide produces only a slight change caused by the salt effect; when the *para*-position is occupied by hydrogen or a nitro-group, however, the mechanism changes to S_N2, and the rate of disappearance of the initial compound is increased considerably by the addition of sodium azide. Table 11 shows the effect of such addition (0.05 M) on the hydrolysis of p-$XC_6H_4CH_2Cl$.

Table 11.

X	MeO	PhO	NO_2	Ph_2CHCl
$\frac{k_{RX}}{k^0_{RX}}$	1.74	20	5430	1.14

The same view arose [329] from a study of the reaction of 1-phenylethyl bromide with potassium and sodium ethoxides in alcohol: the results were described better by competition between $E1$, $E2$, S_N1, and S_N2 mechanisms involving the covalent compound than by Sneen's ion-pair S_N2 mechanism. Analysis of carbon and α-hydrogen isotope effects ($^{12}k/^{14}k$ and k_H/k_D)¶ led to the conclusion [330] that the hydrolysis of benzyl and p-methylbenzyl chlorides in the presence of sodium azide is a classic S_N2 process, while the corresponding reaction of 1-methylheptyl p-bromobenzenesulphonate is described by competition between S_N2 and S_N1 processes with the former predominating.

§ In the cases which they studied, however, the possibility of the formation of a free carbonium ion (by the S_N1 path) is doubtful.

¶ Theory predicts a considerable carbon isotope effect in an S_N2 process, a small effect in an S_N1 process, and the opposite behaviour of the α-hydrogen isotope effect [304].

Thus Sneen's ion-pair S_N2 mechanism has both protagonists and antagonists, and at the present time can be regarded only as debatable [331]. In the Reviewer's opinion recent very significant results have cast doubt on the existence of such a mechanism. Although the chief argument for an ion-pair S_N2 mechanism has been the fractional order with respect to sodium azide, as well as inversion of configuration in the final product, the result may be due to the existence of sodium azide not only as free ions but also as ion-pairs. One author considers [332] that use of concentrations of this salt instead of activities of the azide ion in the kinetic equations is responsible. He showed that such a change will linearise the non-linear relations between k_{obs}/k_{NA} and $[N_3^-]$ in the reaction of 1-methylheptyl methanesulphonate in 25% and 30% aqueous dioxan. However, the slopes of the dependence on $a_{N_3^-}$ of $[RN_3]/[ROH]$ and k_{obs}/k_{NA} differ in both media (addition of sodium azide has a smaller effect on the rate than on the yield—Fig. 4): i.e. there is indeed a difference between the stages determining the rate and the formation of products. However, this difference has been attributed [320] to the occurrence of solvolysis by an intermediate (borderline) mechanism [333]†.

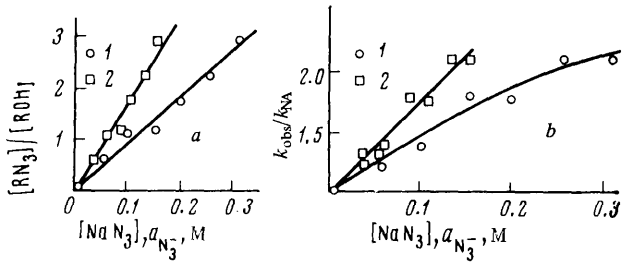


Figure 4. Effect of: 1) concentration of sodium azide; 2) activity of azide ion on reaction of 1-methylheptyl methanesulphonate with sodium azide and water in 30% aqueous dioxan: *a*) ratio of products; *b*) k_{obs}/k_{NA}.

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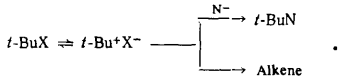
In the present Review we have discussed the involvement of ion-pairs only in S_N reactions, although it has been noted that in secondary systems they are often accompanied by elimination processes. In tertiary systems elimination may become predominant, so that we have almost ignored such systems. Yet in these cases also there are clear indications that ion-pairs, as well as carbonium ions, may take part in the reaction. Thus Winstein et al. [335] showed that, in the solvolysis of t-C_4H_9X compounds in water, a small quantity of an alkene is formed, which is approximately the same for all X, but in a less strongly dissociating solvent (ethanol) the proportion of elimination is sharply increased, and varies significantly with X in the sequence $S(CH_3)_2 < I < Br < Cl$.

† The nature of this mechanism was at one time widely discussed. Cases are known in which the total effect of competing S_N1 and S_N2 mechanisms is unable to describe behaviour characteristic of the "intermediate" region [334].

The yield of alkene in the solvolysis of t-butylethylmethylsulphonium salts in ethanol and in acetic acid increased on passing from the perchlorate to the bromide [336]. All these results were interpreted in terms of ion-pairs:



Finally, we have only mentioned the participation of ion-pairs in reactions at an sp^2-hybridised carbon atom, although study of the solvolytic reactions of the "vinyl cation" is providing increasing evidence of the involvement of ion-pairs even in these reactions [337].

The theoretical foundations of organic chemistry first formulated by Ingold and his school were based mainly on a study of nucleophilic substitution in aliphatic systems, and were then transferred with additions to other types of substitution. There was a period when it seemed that this field, having become classical, was almost exhausted. This was apparent in a change in the number of publications on the theory of nucleophilic substitution and in the increasing attention paid to other types of reactions, which exhibited interesting and novel features. However, as had already happened repeatedly, new ideas and a new standard of research revealed that established views, in this case concerning S_N2 and S_N1 mechanisms, were inadequate. Whatever the fate of the ion-pair S_N2 mechanism, around which heated arguments are currently raging, it is evident that the whole field of nucleophilic substitution will survive the new stage of development, primarily because of the great attention paid by investigators to the role of various types of ionic intermediates. New ideas have led to a new terminology, and writers on mechanisms of solvolytic reactions prefer to speak of the nucleophilic participation of the solvent in the reaction—which is more or less strongly developed depending on the nature of substrate and solvent, and may be completely absent—not about S_N2 and S_N1 mechanisms [313]. The nucleophilic intervention of the solvent in the solvolysis of several secondary systems has been estimated relative to trifluoroacetic acid, whose intervention was equated to zero [338]. The same approach can in principle be extended to other nucleophilic substitutions. However, the new terminology should not conceal the fundamental problem of elucidating the nature of the species involved in the primary stages.

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7,7,8,8-Tetracyanoquinodimethane in Addition, Substitution, and Complex Formation Reactions

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The review is devoted to the properties of 7,7,8,8-tetracyanoquinodimethane, one of the strongest of the known organic π acids. Data concerning the methods of synthesis of 7,7,8,8-tetracyanoquinodimethane and its analogues and the physicochemical properties of compounds of this series are surveyed. The addition, substitution, and complex formation reactions of 7,7,8,8-tetracyanoquinodimethane, its spectroscopic, electrical, and magnetic properties, and the structures of its complexes and radical-ion salts with organic and inorganic electron donors are examined.
The bibliography includes 232 references.

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I. INTRODUCTION

The semiconducting properties of molecular complexes or charge-transfer complexes have been widely investigated in the last 20 years. Although organic semiconductors have not so far found extensive practical applications, in contrast to inorganic semiconductors, interest in these compounds has been stimulated by the synthesis of several new powerful electron acceptors, such as tetracyanoethylene (TCNE), 7,7,8,8-tetracyanoquinodimethane (TCNQ), and tetracyano-*p*-benzoquinone. Although the first two compounds are somewhat inferior as regards their electron-accepting properties to the last, their comparatively easy synthesis led to a vigorous investigation of their chemical properties as well as the physical properties of their complexes.

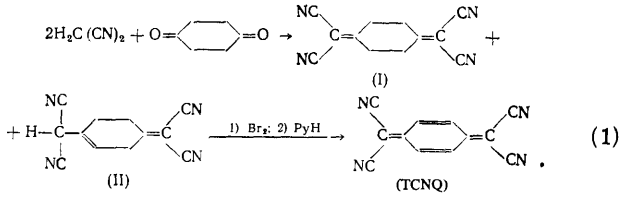
In this connection TCNQ is of particular interest. As a result of the presence in its molecule of four powerful electron-accepting groups, nucleophilic addition reactions, which are rarely encountered among unsaturated compounds, as well as addition reactions proceeding via a one-electron transfer stage are characteristic of this substance. The addition reactions are particularly interesting from the standpoint of modern ideas on the mechanisms of heterolytic substitution reactions. As a result of its powerful electron-accepting properties combined with a comparatively large conjugation system in the molecule (eight π electrons), TCNQ forms a stable radical-anion and gives rise to stable radical-ion salts with many organic and inorganic electron donors, some of which exhibit the highest electrical conductivity observed for organic compounds.

Several TCNQ radical-anion compounds exhibiting "a metallic" temperature variation of the electrical conductivity have been synthesised in recent years. In order to account for the conduction mechanism in such systems, the most modern and fundamental ideas of solid state physics have been resorted to. Thus TCNQ has been the object of intense study by workers in both chemistry and physics.

So far there has been no review dealing with the entire wide variety of properties of both TCNQ itself and its complexes; several of the published reviews deal only with narrow questions concerning the properties of TCNQ complexes. The bibliography on TCNQ and its complexes includes about 600 items. The present review covers the most interesting data relevant to the methods of synthesis and the physicochemical properties of TCNQ and its analogues as well as complexes and radical-ions based on them, which have been published up to the beginning of 1975. Some of the studies on TCNQ, particularly early ones, have been described in reviews which are referred to in the corresponding sections of the present survey.

II. THE SYNTHESIS OF 7,7,8,8-TETRACYANOQUINODIMETHANE AND ITS ANALOGUES AND THEIR PHYSICOCHEMICAL PROPERTIES

Although the reports about the properties of TCNQ complexes refer to 1960, its synthesis was described for the first time in 1962.[1] In the first stage malononitrile is condensed with cyclohexane-1,4-dione and then TCNQ is obtained by bromination and dehydrobromination in the presence of pyridine (in a single stage) [reaction (1)], the overall yield of the product reaching 80%:

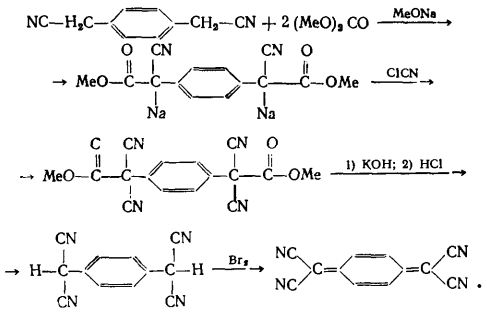


(1)

The first stage may be carried out either in benzene solution in the presence of small amounts of acetic acid and ammonium acetate or in an aqueous medium in the presence of β-alanine. In the first case a mixture of isomers (I) and (II) is formed (this is unimportant for the next stage) in a yield of 75.1%. The second case involves the formation of only isomer (I) in 97% yield. The second stage, the dehydrogenation of compound (I) or a mixture

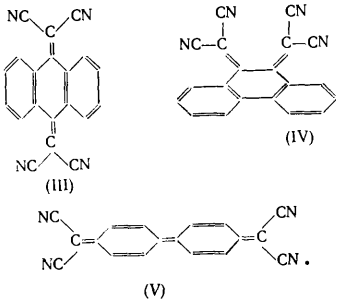
of (I) and (II), may be carried out with the aid of various reagents: *N*-bromosuccinimide, bromine, selenium dioxide, or *N*-chlorosuccinimide; the purest product was obtained by using bromine[1].

Alkyl derivatives of TCNQ were synthesised by a similar procedure: 2-methyl-, 2-propyl-, and 2,5-dimethyl-TCNQ.[2] The starting materials for their synthesis were the alkyl derivatives of cyclohexane-1,4-dione obtained by reducing the corresponding alkyl derivatives of the dimethyl ether of hydroquinone with sodium in liquid ammonia and subsequent demethylation:



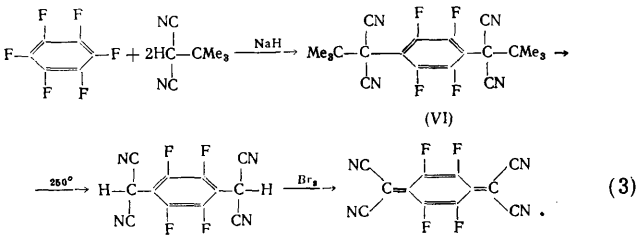
(2)

About 20 TCNQ derivatives with different substituents in the ring (alkyl, alkoxy-, halogeno-, and aryl) have been synthesised by the method based on reaction (2) and on the basis of condensed aromatic hydrocarbons—15,15,16,16-tetracyano-9,10-anthraquinodimethane (III), 15,15,16,16-tetracyano-9,10-phenanthroquinodimethane (IV), and 13,13,14,14-tetracyano-1,12-diphenoquinodimethane (V):[3]



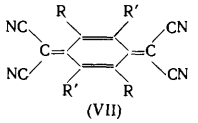
TCNQ was obtained recently (in 80% yields) by the single-stage condensation of cyclohexane-1,4-dione with $(CN)_2CO$ or phosgene in the presence of HCN or NaCN.[4]

The starting materials for the synthesis of 2,3,5,6-tetrafluoro-TCNQ were t-butylmalononitrile and hexafluorobenzene, which in the presence of sodium hydride give rise to the condensation product (VI), the latter being converted into 2,3,5,6-tetrafluoro-TCNQ after hydrolysis and treatment with an excess of bromine [reaction (3)]:[5]



(3)

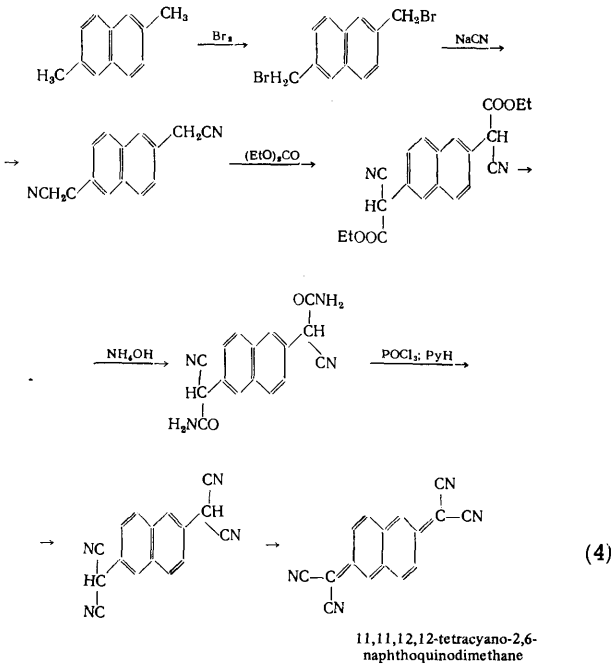
A whole series of substituted TCNQ derivatives (VII) were obtained using polyhalogeno- and cyano-benzenes[5]:



(a) R=H, R'=CN; (b) R=F, R'=CN; (c) R=R'=CN; (d) R=H, R'=F; (e) R=F, CN; R'=F; (f) R=F, CN, R'=CN; (g) R=F, H, R'=F.

Two naphthalene analogues of TCNQ have been synthesised: 11,11,12,12-tetracyano-1,4-naphthoquinodimethane and 11,11,12,12-tetracyano-2,6-naphthoquinodimethane. The former was obtained from *cis*-2,3,5,8,9,10-hexahydro-1,4-naphthoquinone via reaction (1).[6]

The synthesis of 11,11,12,12-tetracyano-2,6-naphthoquinodimethane is much more complex [reaction (4)].[2] The starting material for this purpose was 2,6-dimethylnaphthalene into which four CN groups were introduced in succession: the abstraction of two methine hydrogen atoms led to a common system of conjugated double bonds in the molecule. 11,11,12,12-Tetracyano-2,6-naphthoquinodimethane was synthesised recently also via reaction (2) and the method of preparation of the initial 2,6-naphthylenedimalononitrile was considerably improved[7]:



(4)

11,11,12,12-tetracyano-2,6-naphthoquinodimethane

The interaction of diphenyldiazomethane with TCNQ leads to 2-diphenylmethyl-TCNQ.[8]

Data on the electron-accepting capacity of TCNQ, its analogues, and derivatives (and for comparison of TCNE[9]) are presented in Table 1. The principal characteristic of the strength of the acceptor is its electron affinity E_A. The values of E_A for TCNQ and TCNE, determined by the magnetron method, are 2.75 and 2.76 eV respectively[10].

Another widely used method for the determination of E_A is based on the proportionality of the electron affinity of the acceptor to the half-wave potential in its polarographic titration. The E_A for 11,11,12,12-tetracyano-1,4- and 11,11,12,12-tetracyano-2,6-naphthoquinodimethanes were determined in this way[6]. Since there are no E_A values in the literature for the remaining acceptors, we quote here the literature data for polarographic titration under standard conditions: in 0.1 M lithium perchlorate solution in acetonitrile relative to the saturated calomel electrode.

It follows from the data in Table 1 that the introduction of fluorine or the CN group enhances sharply the electron-accepting properties of TCNQ. Alkyl derivatives of TCNQ as well as 11,11,12,12-tetracyano-1,4-naphthoquinodimethane are clearly weaker electron acceptors (particularly the latter) than TCNQ itself. According to X-ray diffraction data, the CN groups in 11,11,12,12-tetracyano-1,4-naphthoquinodimethane are not in the same plane as the naphthalene ring owing to the steric interaction with the hydrogen atoms in the 5- and 8-positions[11]. In the electronic spectrum of 2-diphenylmethyl-TCNQ the absorption band exhibits a fairly considerable hypsochromic shift (Table 1), which indicates a non-planar conformation of its molecule. However, all the TCNQ derivatives listed in Table 1 are fairly powerful electron acceptors and form complexes and radical-ion salts with organic and inorganic electron donors[2,6]. Since all the electron acceptors have similar structures, we shall henceforth consider only TCNQ, because investigators have concentrated attention on its properties and those of its complexes.

Table 1. The properties of TCNQ and its derivatives ($E_{1/2}^{-}$ and $E_{1/2}^{=}$ are the half-wave potentials in polarographic titration with formation of an anion and dianion respectively; E_A is the electron affinity).

Acceptor	M.p., °C	$E_{1/2}^{-}$, V	$E_{1/2}^{=}$, V	λ_{max}, nm($10^{-4}\epsilon$)	eV	Refs.
3,6-Dicyano-2,5-difluoro-TCNQ		+0.75	+0.23	—	—	5
2,5-Dicyano-TCNQ		+0.07	+0.07	—	—	5
2,3,5,6-Tetrafluoro-TCNQ	295—300	+0.52	+0.03	—	—	5
11,11,12,12-Tetracyano-2,6-naphthoquinodimethane	>420	+0.21	−0.17	248 (1.8) 258 (1.4) 472 (8.7)	1.65*	2
TCNE	199—200	+0.15	−0.57	265	2.76**	9
TCNQ	296—298	+0.14	−0.29	395 (6.36)	2.75**	1
2,5-Diisopropyl-TCNQ	—	+0.12	−0.38	—	—	2
2-Methyl-TCNQ	200—201	+0.12	−0.26	396 (6.0)	—	2
2-n-Propyl-TCNQ	125—127	+0.10	−0.31	397 (6.0)	—	2
2,5-Dimethyl-TCNQ	265—267	+0.02	−0.28	403 (6.0)	—	2
11,11,12,12-Tetracyano-1,4-naphthoquinodimethane	244—245	−0.088	−0.36	288 (6.9) 392 (3.47) 409 (3.3)	1.49*	6
2-Diphenylmethyl-TCNQ	350—353	—	—	361 (2.56) 258 (0.665) 221 (1.77)	—	8

*Chatterjee's data[6].
**Farragher and Page's data[10].

TCNQ is a crystalline yellow-brown substance melting at 296—298°C and subliming readily above 250°C. In the solid state it is stable in air but in solutions it is sensitive to moisture[1]. According to X-ray diffraction data, the TCNQ unit cell has the following parameters: $a = 8.906$ Å, $b = 7.060$ Å, $c = 16.395$ Å, and $\beta = 98.54°$; its density is 1.315 g cm^{-3}. The bond lengths and angles in the TCNQ molecule are shown in Fig. 1. The distance between the planes of adjacent molecules in the crystal is 3.45 Å.[12]

The electronic spectrum of the acetonitrile solution of TCNQ shows one absorption band (395 nm, $\epsilon = 6.36 \times 10^4$)[1]; four maxima, at 304, 341, 402, and 424 nm, were found for the single crystal in polarised light along the a and b axes[13]. Quantum-chemical calculations on the TCNQ molecule[14-17] lead to a system of electronic transitions consistent both with the experimentally observed electronic absorption bands and with the photoelectronic spectra of TCNQ.[18,19]

The infrared[20-22] and Raman[23] spectra of TCNQ have been investigated in detail. The most intense infrared lines are at 3050 [ν(C—H)], 2220 [ν(C≡N)], 1540 [ν(C=C)], 1545 {ν[C=C(CN$_2$)]}, and 861 cm^{-1} [γ(C—H)] and in the Raman spectrum the most intense lines are at 3050 [ν(C—H)], 2225 [ν(C≡N)], 1602 {ν[C=C(CN)$_2$]}, 1554 [ν(C=C)], and 1210 [δ(C—H)].

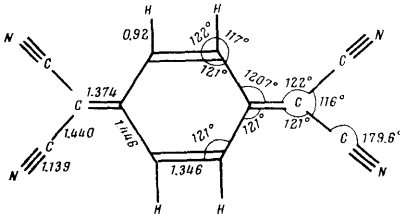


Figure 1.

According to ^{14}N nuclear quadrupole resonance data, the nitrogen atoms in the TCNQ molecule can occupy two non-equivalent positions. The average frequency of the quadrupole interaction constant is 4021 kHz for TCNQ. The observed asymmetry in the position of the nitrogen atoms can be explained by the non-equivalence of the polarisation of the π orbitals of the nitrile group parallel and at right angles to the plane of the ring[24].

According to its electrical properties, the TCNQ single crystal is a typical organic semiconductor (the conductivity at 20°C is 2×10^{-12} Ω^{-1} cm^{-1} and the activation energy for dark conduction is 0.6 eV [25-27]). Furthermore, TCNQ single crystals exhibit photoconduction[25,26]. Measurements of the electrical characteristics of TCNQ single crystals prepared in different ways showed that the single crystals, both grown *in vacuo* and obtained on cooling solutions, contain an admixture of the sodium salt of TCNQ owing to the leaching of glass; the dark conductivity is relatively insensitive to this impurity, while the photoconductivity depends strongly on its concentration[26].

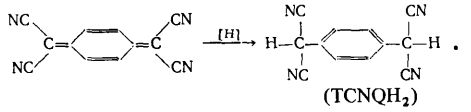
A special investigation of the influence of the admixture of the lithium salt of TCNQ on the electrical properties of TCNQ itself revealed the opposite effect of this additive: 1—2% of the salt impurity increased the dark current but hardly affected the photoconductivity[27]. This difference between the effects of impurities can probably be accounted for by their amount: whereas in the first instance we are probably dealing with 0.1—0.01%, in the second the concentration of the impurity is 1—2%.

III. CHEMICAL PROPERTIES

1. Addition Reactions

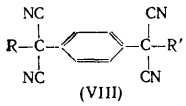
Whereas 1,4-addition reactions in which 3-substituted hydroquinones are formed are characteristic of p-benzoquinone, a structural analogue of TCNQ, 1,6-addition reactions are characteristic of TCNQ. The simplest example of such a reaction is the reduction of TCNQ by

thiophenol, mercaptoacetic acid, or hydriodic acid with formation of *p*-phenylenedimalononitrile ($TCNQH_2$): [1]



($TCNQH_2$)

TCNQ readily reacts with sulphur dioxide in aqueous acetonitrile to form the sulphonic acid (VIIIa). [1] In the absence of catalysts TCNQ does not react with halogens: in the reaction with chlorine in the presence of catalytic amounts of triethylamine or NMe_4Cl, the dichloro-derivative (VIIIb) was obtained:



(VIII)

(a) R=H, R′=SO_3H; (b) R=R′=Cl; (c) R=R′=Br; (d) R=R′=C(Me)$_2$CN; (e) R=H, R′=4-$C_6H_4NR''_2$; (f) R=H, R′=4-OH-2-R″C_6H_3; (g) R=H, R′-2-pyrrolyl; (h) R=H, R′=3-indolinyl; (i) R=H, R′-1-azulenyl; (j) R=HgOAc, R′=4-$C_6H_4NMe_2$.

The analogous bromo-derivative (VIIIc) is formed only when bromine interacts with the disodium salt of $TCNQH_2$.

The addition product (VIIId) was isolated in the thermal decomposition of $\alpha\alpha'$-azobisisobutyronitrile in the presence of TCNQ.

NN-Dimethylaniline also forms a 1,6-addition product (VIIIe, R″ = Me) with TCNQ. [1] A more detailed study of the interaction of TCNQ with a series of aromatic amines [28,29] showed that only the *para*-position relative to the amino-group is active in this reaction even in the case of amines such as *NN*-dimethyl-1-naphthylamine. A series of addition products (VIIIe) with R″ = H, Me, Et, Pr, Bu, or Ph were obtained. The only aromatic amines which react with TCNQ are those whose ionisation potential I_D is less than 7.8–8.0† eV or, what amounts to the same thing, amines which form complexes with TCNQ whose spectra contain a charge-transfer band above 600 nm (in chloroform).

TCNQ reacts with phenols very slowly to form compounds (VIIIf). The use of sodium phenoxide leads to an appreciable acceleration of the reaction [31]. This is apparently associated with the fact that the electron-donating properties of phenols are inadequate ($I_D > 8$ eV) and only phenoxide ions, the concentration of which is extremely low under the usual conditions (in acetonitrile), are involved in the reaction.

Pyrrole and indole react with TCNQ to form addition products (VIIIg) and (VIIIh) respectively. If the 2- and 5-positions in pyrrole are occupied, the 3- or 4-position is reactive. If the 3-position in indole is occupied, substitution takes place in the 2-position, but the reaction proceeds under more severe conditions [31].

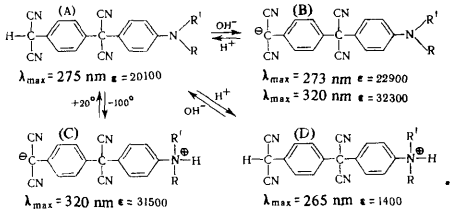
In acetonitrile TCNQ reacts readily with azulene; as in the case of TCNE, [32] this involves the formation of 1-substituted azulene derivatives (VIIIi). [33] An organomercury compound (VIIIj) was obtained by the reaction of TCNQ with *p*-*NN*-dimethylaminophenylmercury acetate [28].

It is noteworthy that, whereas the reactions involving the addition of chlorine and sulphur dioxide resemble nucleophilic reactions involving addition to the double bond and the addition of the dimethylacetonitrile radical resembles radical addition reactions, the interaction with aromatic amines, phenols, nitrogen-containing heterocycles, azulene, and *p*-dimethylaminophenylmercury acetate apparently begins with the addition of the electron donor to TCNQ with formation of the radical-ion TCNQ salt; the site where a hydrogen atom is substituted in the donor molecule is similar to that in electrophilic substitution under mild conditions [28]. The formation of $TCNQH_2$ in the reaction of TCNQ with triarylphosphine proceeds in accordance with this mechanism via the intermediate $TCNQ^{\cdot}$ radical-anion:

$$Ar_3P + TCNQ + H_2O \xrightarrow{H^+} Ar_3PO + TCNQH_2 .$$

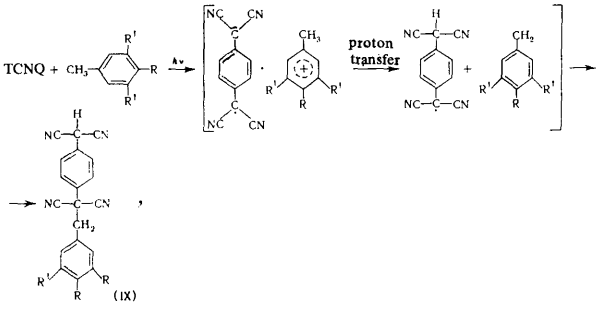
This was demonstrated in a kinetic study of the reaction using optically active arylphosphines [35].

The majority of compounds (VIII) contain the acid malononitrile hydrogen atom, which can be readily split off: as a result, these compounds are sensitive to the pH of the medium. This is particularly clearly seen for compounds (VIIIe), which can exist in four different forms in solution, differing in their electronic absorption spectra and capable of being reversibly converted into one another [reaction (5), compound (VIIIe), R = R′ = CH_3; (A) = undissociated compound, (B) = anion, (C) = inner salt, (D) = ammonium salt] [36]:



(5)

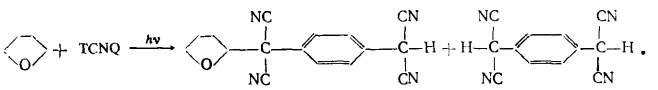
On illumination with light corresponding to the charge-transfer band of the TCNQ complexes with toluene, *p*-xylene, and mesitylene, compounds having the general formula (IX) are formed, probably via a stage involving the photoinduced addition of a proton to TCNQ: [37]



(IX)

where R and R′ = H or Me.

Yet another example of radical addition to TCNQ is its interaction with tetrahydrofuran:



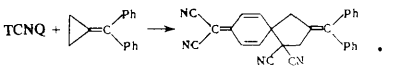
The reaction proceeds when a mixture of the initial compounds is illuminated by ultraviolet light or in the presence of peroxides [38].

In contrast to *p*-benzoquinone [39], TCNQ does not form Diels–Alder adducts with dienes: the reaction with cyclopentadiene and methylbuta-2,3-diene results in the formation of a polymeric product only [1].

An unusual reaction involving addition to TCNQ was discovered recently [40]. When TCNQ interacts with

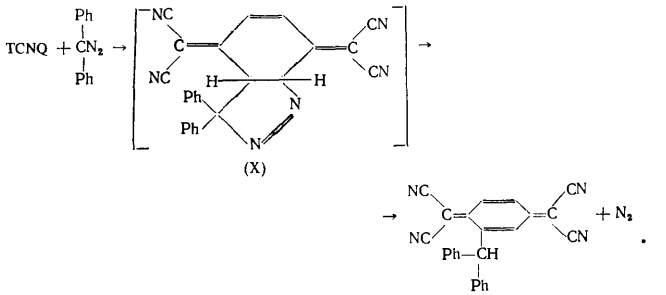
† The ionisation potential was determined by the photoionisation method; other methods give a somewhat higher value of I_D.

2,2-diphenylmethylenecyclopropane, the addition product with the structure shown below is formed in 60% yield:



2. Substitution Reactions

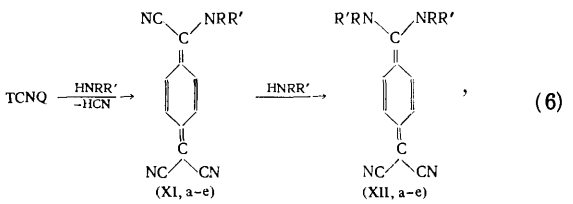
In principle two types of substitution reactions with TCNQ are possible: the substitution of hydrogen and of CN groups. The only example of reactions of the first type is the interaction of TCNQ with diphenyldiazomethane already mentioned [8]:



(X)

This involves the formation of 2-diphenylmethyl-TCNQ, probably via the intermediate cyclic derivative (X).

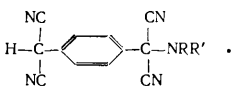
Among reactions of the second type, mention may be made of the interaction of TCNQ with primary and secondary aliphatic and aromatic amines [reaction (6)]: [41]



(XI, a-e) (XII, a-e) (6)

where R = R′ = H (a), R = H and R′ = Bu (b), NRR′ = *N*-pyrrolidinyl (c), R = H and R′ = 4-C_6H_4OMe (d), and R = H and R′ = NH_2 (e).

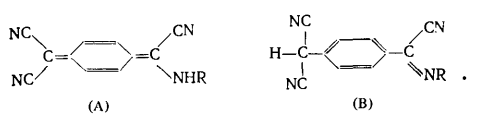
It is noteworthy that the reactions involving substitution of the cyano-groups in TCNQ apparently proceed via the formation of an intermediate product of 1,6-addition to the quinonoid system of TCNQ [compound (XIII)], which splits off HCN rapidly at room temperature and is converted into the corresponding compound (XI):



(XIII)

The spectra of intermediates of type (XIII) were observed for films, obtained by the simultaneous sputtering of TCNQ and electron donors (*p*-phenylenediamine or *m*-phenylenediamine) onto a support cooled to 77 K, when the film was heated slowly to room temperature [42].

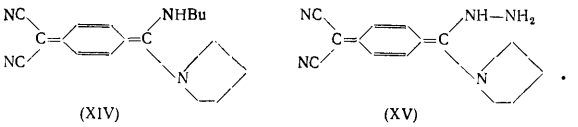
Aliphatic compounds (XI) [for example (XIb)] exist in the form of two isomers—(A) and (B): [41]



(A) (B)

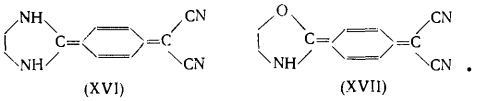
The *p*-anisidine derivative (XId) was obtained only in form (B). [41] Judging from the electronic spectra, *p*-phenylenediamine also gives rise to form (B), while *m*-phenylenediamine reacts with formation of the quinonoid form (A). [42]

Mixed derivatives of TCNQ have also been obtained by reaction with amines [compounds (XIV) and (XV)] [41]:



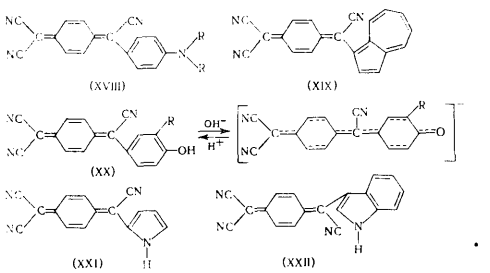
(XIV) (XV)

Bifunctional amines (for example, ethylenediamine and monoethanolamine) are capable of substituting two cyano-groups in TCNQ [compounds (XVI) and (XVII)] [41]:



(XVI) (XVII)

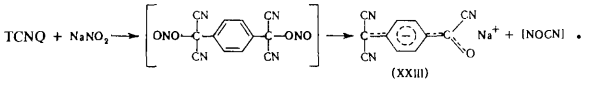
The products of the substitution of a cyano-group in TCNQ [compounds (XVIII)–(XXII)] have been obtained by ultraviolet irradiation of the corresponding products of the 1,6-addition reaction [compounds (VIII, e–i)]. They all have a deep colour (red for the product of the reaction with phenol and blue for all others); the position of their long-wavelength absorption band depends on the nature of the electron-donating group and varies from 500 to 700 nm. The absorption band itself is due to intramolecular charge-transfer [29,31,33]:



(XVIII) (XIX) (XX) (XXI) (XXII)

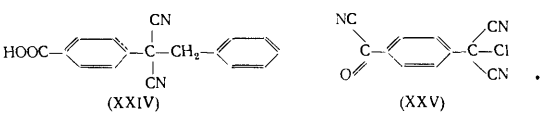
Compound (XX) contains an acid proton, which splits off reversibly in an alkaline medium to form an intensely blue anion [31].

Another example of substitution reactions of TCNQ is its interaction with sodium nitrite, which leads to the formation of an orange-red salt (XXIII) via a hypothetical intermediate addition product:



(XXIII)

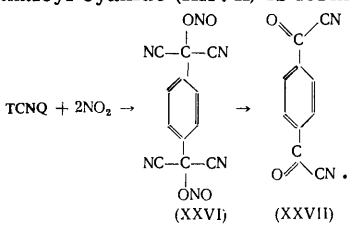
Like chlorination, benzylation of the salt (XXIII) (followed by hydrolysis) leads to the formation of the addition products (XXIV) and (XXV) respectively [41]:



(XXIV) (XXV)

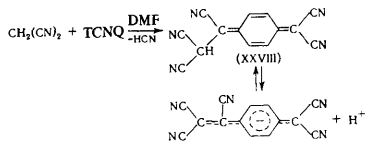
N_2O_4 reacts with TCNQ similarly to $NaNO_2$. When the reaction was carried out in acetonitrile at 0°C, an unstable intermediate, to which structure (XXVI) was attributed,

was obtained in 75% yield. On heating it *in vacuo* at 130°C, terephthaloyl cyanide (XXVII) is formed[41]:



(XXVI) (XXVII)

The substitution product (XXVIII) was obtained by the reaction of TCNQ with malononitrile in dimethylformamide (DMF):[43]



(XXVIII)

Compound (XXVIII) is a strong acid ($pK_a = 0.60$) and readily dissociates in solution to form an intensely blue carbanion; in strongly acid solutions, where the dissociation is suppressed, the colour of compound (XXVIII) differs little from that of TCNQ. Thus nucleophilic reactions involving 1,6-addition to the conjugated double bond system, which in many instances are the first stage of the CN substitution reactions, are most characteristic of TCNQ. The mechanism of these processes has been inadequately investigated, although it is of definite interest, since in some cases the reaction apparently proceeds via one-electron oxidation of the donor with formation of an intermediate radical-ion salt.

3. Complex Formation Reactions

The ability of quinones to form stable solid complexes with aromatic amines has been known for a long time[44]. TCNQ, a strong π acid, forms three types of complexes with electron-donating compounds[45]. Since these complexes are of much interest from the standpoint of their semiconducting properties, the dark conductivities σ are listed below as their characteristics. The first type includes classical molecular complexes in which mainly aromatic hydrocarbons are used as electron donors ($\sigma = 10^{-3}-10^{-14}\ \Omega^{-1}\ cm^{-1}$, Table 2).[45]

The second type of TCNQ complexes includes simple radical-ion salts having the general formula $M^{n+}(TCNQ^{\cdot-})_n$, where M^{n+} is a metal cation or organic cation with n charges, which represent the limiting case of molecular complexes: here the electron is completely transferred from the donor to the acceptor molecule ($\sigma = 10^{-4}-10^{-12}\ \Omega^{-1}\ cm^{-1}$).[45] We may note that such compounds are referred to in the literature as both strong complexes and as simple radical-ion salts. The electronic spectra of their solutions contain the absorption bands of the donor radical-cations and the $TCNQ^{\cdot-}$ radical-anion.

The third type of TCNQ complexes includes complex radical-ion salts having the general formula $M^+(TCNQ^{\cdot-}) \cdot (TCNQ^0)$, or $M^{2+}(TCNQ^{\cdot-})_2 \cdot (TCNQ^0)$. In solution these salts dissociate with formation of the donor cation, the $TCNQ^{\cdot-}$ radical-anion, and the neutral molecule $TCNQ^0$. However, in the crystal the electron is delocalised over both acceptor molecules and the radical-anion is of the form $(TCNQ^{\cdot-})_2$. As a rule these salts give rise to an intense ESR signal; their spin concentration may reach 1–1.5 spins per donor–acceptor pair. The complex radical-ion salts have a strikingly high conductivity[45]: $\sigma = 10^{-3}-10^{2}\ \Omega^{-1}\ cm^{-1}$.

It is noteworthy that there is no sharp boundary between weak molecular complexes and radical-ion salts. Thus the complex of TCNQ and *NNN'N'*-tetramethyl-*p*-phenylenediamine dissociates in acetonitrile with formation of a radical-ion pair[45].

Table 2. Molecular TCNQ complexes with aromatic donors[45].

Donor	Solvent used in synthesis	Yield, %	M.p., °C	Resistivity, Ω cm	λ_{max} of charge-transfer band, nm
NNN'N'-Tetramethyl-*p*-phenylenediamine	$CHCl_3$	71	128—129	10^6	1163[a]
NN-Dimethyl-*p*-phenylenediamine	$CHCl_3$	38	112—117	10^9	
Diaminodurene	THF	86	190 decomp.	10^9	
1,5-Diaminonaphthalene	$CHCl_3$	59	197 decomp.	10^9	
Anthracene	THF	42	282—283	10^{11}	845[b]
Pyrene	THF	52	260 decomp.	10^{12}	765[b]
Hydroquinone[c]	THF		180—185		
4,6,8-Trimethylazulene	THF	85	160—167	10^9	

[a] Kosower's data[46]. [b] Beukers and Szent-Gyorgyi's data[47]. [c] Molar ratio donor : TCNQ = 1 : 2.

A comparative study of the electronic spectra of a solution of this complex relative to those of the perchlorate of Wurster's Blue and the lithium salt of TCNQ showed that it is dissociated to an extent greater than 80%. The study of the polarisation absorption spectra of single crystals of the complex confirmed its partially ionic character[48]. Similar conclusions were reached also about the structure of TCNQ complexes with *NNN'N'*-tetramethylbenzidine and benzidine[49].

Table 3. TCNQ complexes forming clathrate compounds with solvents[50,51].

Donor	Solvent	Donor : acceptor : solvent molar ratio	Donor	Solvent	Donor : acceptor : solvent molar ratio
Benzidine	CH_2Cl_2	1,0:1,1:1,6	3,3'-Dichlorobenzidine	CH_2Cl_2	1,0:0,8:0,16
Benzidine	C_2H_5Br	1,0:1,1:1,6		CH_2Cl_2	1,0:1,0:0,23
Benzidine	MeCOMe	1,0:0,8:0,8	*o*-Toluidine	$CHCl_3$	1,00:1,07:0,52
3,3'-Diaminobenzidine	CH_2Cl_2	1,0:1,0:0,45	*o*-Toluidine		

It was found that certain solvents form clathrate compounds with TCNQ complexes (Table 3)[50,51]. Their crystal structures[52] and electrical properties[53] have been investigated.

The ability of TCNQ to undergo readily one-electron reduction under the influence of certain metals, metal iodides, or the iodides of organic cations has been used to synthesise simple TCNQ radical-ion salts[45]. Thus copper or silver readily react with TCNQ in acetone or acetonitrile at room temperature:

$$Cu + TCNQ \rightarrow Cu^+ TCNQ^{\cdot-},$$

$$Ag + TCNQ \rightarrow Ag^+ TCNQ^{\cdot-},$$

$$MI + TCNQ \rightarrow M^+ TCNQ^{\cdot-} + \frac{1}{2} I_2,$$

where M is the metal or organic cation.

It has been shown that the TCNQ + $I^- \rightleftharpoons TCNQ^{\cdot-} + \frac{1}{2}I_2$ system is reversible. The standard reduction potential of TCNQ is 0.581 V relative to the standard hydrogen electrode[54].

There are several ways of synthesising simple radical-ion TCNQ salts[45]. The first procedure (*a*) involves the interaction of metal iodides with TCNQ. TCNQ salts with lithium, sodium, potassium, copper, etc. have been obtained in this way. The maximum yield of the salt is reached when the reactant ratio corresponds to the equation

$$3LiI + 2\ TCNQ \rightarrow 2Li^+TCNQ^{\cdot-} + Li^+ + I_3^- .$$

In the second method (*b*) TCNQ radical-ion salts are obtained by the exchange reaction between the lithium salt of TCNQ, which is readily soluble in water or acetonitrile, with a soluble metal salt or the salt of an organic cation. Examples of the syntheses of certain salts by this procedure[47] are presented below:

$$Li^+\ TCNQ^{\cdot-} + FeSO_4 \xrightarrow{H_2O} Fe^{++}(\ TCNQ^{\cdot-})_2 \cdot 3H_2O ,$$

$$Li^+\ TCNQ^{\cdot-} + AgNO_3 \xrightarrow{H_2O} Ag^+\ TCNQ^{\cdot-} , \qquad (7)$$

$$Li^+\ TCNQ^{\cdot-} + Et_3NH^+I^- \xrightarrow{CH_3CN} Et_3NH^+\ TCNQ^{\cdot-} ,$$

$$Li^+\ TCNQ^{\cdot-} + \text{(N-Me iodide)} \xrightarrow{CH_3CN} \text{(N-Me TCNQ}^{\cdot-}\text{ salt)} .$$

Table 4. The constants and methods of synthesis of simple TCNQ salts.

Cation	Method of synthesis	Solvent	Yield, %	Decomp., temp., °C	Resistivity, Ω cm
Li^+	(*a*)	CH_3CN	98	>300	$2\cdot10^5$
Na^+	(*a*)	CH_3CN	59	>300	$3\cdot10^4$
K_+	(*a*)	CH_3CN	70	>300	$5\cdot10^3$
Cs^+	(*b*)	CH_3CN	67	—	$3\cdot10^4$
Ba^{++}	(*a*)	CH_3CN	70	—	$8\cdot10^5$
Cu^+	(*a*)	CH_3CN	54	—	$2\cdot10^2$
Cu^{++}	(*b*)	CH_3CN	80	—	$2\cdot10^2$
$Cu(NH_3)_2^{++}$	(*b*)	CH_3CN	94	—	$7\cdot10^2$
NH_4^+	(*a*)	THF–MeOH	60	210—215	$6\cdot10^4$
Et_3NH^+	(*b*)	H_2O	81	~180	10^9
$(n\text{-}Bu)_4N^+$	(*b*)	H_2O	—	135	10^{12}
Morpholinium	(*a*)	CH_3CN	35	~220	10^9
$Ph_3(Me)P^+$	(*b*)	H_2O	99	~170	$4\cdot10^{10}$
Pyridinium	(*c*)	CH_3CN	59	158—195	10^8
N-Methylpyridinium	(*b*)	CH_3CN—EtOH	—	~235	10^5
N-Methylquinolinium	(*b*)	CH_3CN—EtOH	76	240—244	10^7
5,8-Dihydroxyquinolinium	(*d*)	$CHCl_3$	72	168—169	15

The third method (*c*), the interaction of an amine with $TCNQH_2$ and with TCNQ, has been considered in detail in connection with the synthesis of complex TCNQ salts [see reaction (9)] and the fourth method (*d*) involves the direct interaction of an amine with TCNQ. Table 4 presents data concerning the method of synthesis and certain characteristics of a number of simple TCNQ salts[45].

The methods of synthesis of complex TCNQ radical-ion salts are illustrated by Eqn. (8) for the synthesis of a complex triethylammonium radical-ion salt (XXIX) (the yield of the salt is indicated in brackets)[45]:

$$\text{(a)}\ Et_3NH^+\ TCNQ^{\cdot-} + TCNQ \rightarrow Et_3NH^+(\ TCNQ)_2^{\cdot-}\ \text{(XXIX)}\ \ (50\%) ,$$
$$\text{(b)}\ 3Et_3NH^+I^- + 2\ TCNQ \rightarrow \text{(XXIX)}\ \ (50\%) , \qquad (8)$$
$$\text{(c)}\ 2Et_3N + TCNQH_2 + 3\ TCNQ \rightarrow \text{(XXIX)}\ \ (90\%) ,$$
$$\text{(d)}\ Et_3N + 2\ TCNQ \rightarrow \text{(XXIX)}\ \ (77\%) .$$

In the first method (*a*) one mixes hot solutions of a simple TCNQ salt and neutral TCNQ; the complex TCNQ salt crystallises on cooling. This method is used when the complex salt is much less soluble in the given solvent than the simple salt.

In the second method (*b*) the complex salt is obtained from TCNQ and a metal iodide or the iodide of an organic cation, the iodide ion reducing TCNQ.

In the synthesis of complex TCNQ salts by the third method (*c*), the starting materials are TCNQ and $TCNQH_2$ [reaction (9)]:

$$R_3N + TCNQH_2 \rightarrow R_3NH^+ + TCNQH^- \longrightarrow R_3NH^+ + TCNQ^{\cdot-} + TCNQH^{\cdot}$$
$$\downarrow R_3N \qquad 2R_3NH^+ + 2\ TCNQ^{\cdot-} \quad \downarrow 2TCNQ \quad \leftarrow R_3N \qquad (9)$$
$$2R_3NH^+ + TCNQ^- \downarrow TCNQ$$
$$2R_3NH^+ + 2TCNQ^{\cdot-} \xrightarrow{2\ TCNQ} 2\,[R_3NH^+(\ TCNQ)_2^{\cdot-}] .$$

In one of the versions of this method (*b'*) durohydroquinone is used as the proton and electron donor:

$$2 \times \text{(quinoline)} + \text{(durohydroquinone)} + 4\ TCNQ \rightarrow$$
$$2\,[\text{(quinolinium)}^+(TCNQ)_2^{\cdot-}] + \text{(durosemiquinone)} .$$

Table 5. The constants and methods of synthesis of certain complex TCNQ salts.

Cation	Method of synthesis	Solvent	Yield, %	Decomp. temp., °C	Resistivity, Ω cm
$(Et)_3NH^+$	(*d*)	THF	77	>195	20
	(*a*)	CH_3CN	32	—	—
	(*c*)	CH_3CN	62	—	—
$(Me)_3NH^+$	(*d*)	THF	90	>215	$5\cdot10^6$
$(Et)_4N^+$	(*a*)	CH_3CN	79	255—268	$2\cdot10^4$
Cs^+ *	(*a*)	CH_3CN	82	—	$9\cdot10^4$
Morpholinium*	(*a*)	CH_3CN	40	210	10^5
Pyridinium	(*c*)	CH_3CN	42	168—185	37
Quinolinium	(*b*)	CH_3CN	91	~250	0.5
	(*b*)	CH_2Cl_2	44	—	—
	(*c*)	CH_3CN	87	—	—
	(*c'*)	CH_3CN	71	—	—
N-Methylquinolinium	(*a*)	CH_3CN	22	245—250	3
N-Ethylquinolinium	(*a*)	CH_3CN	—	237—239	8
Ferricinium	(*d*)	CH_3CN	—	—	0,24
$Ph_3(Me)P^+$	(*a*)	CH_3CN	60	231—233	60; 600; 10^{5}**
Ph_4P^+	(*a*)	CH_3CN	33	228—237	10^3; 10^6; $2\cdot10^{6}$**
$Ph_3(Me)As^+$	(*a*)	CH_3CN	56	224—227	57; 900; 10^{5}**
Ph_4Sb^+	(*a*)	CH_3CN	42	219—220	13; 1.5; 10^4; **

*The composition of the complex was $(cation^+)_2.(TCNQ^{\cdot-})_2$. .TCNQ, while in the remaining cases the composition was $(cation^+).(TCNQ^{\cdot-}).TCNQ$.

**The resistivities of single crystals in three crystallographic directions are quoted.

The fourth method (*d*) is used to synthesise complex salts of TCNQ and aliphatic amines. The solvent apparently serves as the proton donor in this case, although the reaction mechanism has not been elucidated[45]. Data concerning the synthesis and properties of complex TCNQ radical-ion salts are presented in Table 5.

New methods for the synthesis of TCNQ salts have been described recently. Thus thin polycrystalline films of alkali metal (M) salts of TCNQ having the 1 : 1 (M = Li, Na, K, or Rb) and 2 : 3 (M = Cs) compositions were obtained by the successive vacuum sputtering of the metal and TCNQ.[54]

The interaction of TCNQ with distannane leads to the oxidation of the latter and the formation of a radical-ion salt[55]:

$$R_3Sn{-}SnR_3 + 2TCNQ \xrightarrow{THF} 2\,(R_3Sn)^+\,(TCNQ)^-,$$

where R = Me or Bu.

Although the following reaction can hardly be regarded as a method for the synthesis of the radical-ion salts, it too leads to the formation of a salt[56]:

$$2Ph{-}C{\equiv}CCu + 2TCNQ \rightarrow 2Cu^+\,(TCNQ)^- + Ph{-}C{\equiv}C{-}C{\equiv}C{-}Ph\ .$$

There is an extensive literature on the synthesis of TCNQ complexes and salts, but we shall consider only reports of studies which in our opinion are of greatest interest and which make it possible to illustrate the wide variety of electron-donating compounds employed.

TCNQ complexes with aminoazo-dyes have been investigated[57]. Numerous simple and complex TCNQ salts with cationic dyes (primarily cyanine dyes) have been studied[58-60] and simple and complex TCNQ salts with *N*-methylpyrazine and its benzo-derivatives[61], with hydroxy- and halogeno-derivatives of piperidine and pyrrolidine[62], and with polyepichlorohydrin[63] have been synthesised. Simple and complex TCNQ salts with arenechromium compounds (for example with dibenzenechromium) have been obtained[64] and numerous TCNQ complexes with *p*-aminobenzenesulphonamide and its derivatives have been investigated[65]. TCNQ radical-ion salts with cobalt complexes[66], platinum, palladium, and nickel complexes[67], and copper, iron, and nickel chelates[68] have been synthesised.

Ternary (1 : 1 : 1) TCNQ complexes with dyes containing the molecule of a second acceptor [iodine[69] and 9-dicyanomethylene-2,4,7-trinitrofluorenone (XXX)] have been investigated[70]. The latter complex dissociates in solution into the dye cation, the TCNQ anion, and the neutral molecule of compound (XXX). The structure of this complex consists of a collection of parallel stacks of the donor and the acceptor, the TCNQ and (XXXX) molecules alternating in the acceptor stack[71].

IV. PHYSICOCHEMICAL PROPERTIES OF 7,7,8,8-TETRACYANOQUINODIMETHANE COMPLEXES

1. Crystal Structure

Both the optical and electrical properties of TCNQ complexes depend directly on their crystal structure and for this reason we shall consider initially the structures of solid TCNQ complexes. Since data on the structures of the complexes have been recently surveyed in a review[72], we shall only briefly enumerate the principal characteristics of the structures of TCNQ complexes, including the results of studies in recent years.

Molecular TCNQ complexes have a structure which differs sharply from that of the radical-ion salts. Like complexes containing other well-known electron acceptors, they consist of infinite stacks in which donor and acceptor molecules alternate. The molecular planes of the donor and acceptor are approximately parallel and the distances between them (3.4–3.7 Å) are typical for weak intermolecular bonds (Table 6). The bond lengths and the valence angles in the molecules hardly change under these conditions. It has recently been found[76] that there is a direct proportionality between the donor–acceptor distance in TCNQ molecular complexes and the difference between the ionisation potential of the donor and the electron affinity of the acceptor (after Briegleb[82]).

Table 6. The donor–acceptor distances in TCNQ complexes.

Donor	Donor-acceptor distance, Å	References
Hexamethylbenzene	3.65	72
Anthracene	3.50	72
Acenaphthene	3.35	73
Pyrene	3.50	74
Perylene	3.44	75
Phenazine	3.38	76
Phenothiazine	3.52	77
1,10-Phenanthroline	3.45	78
Dibenzo-*p*-dioxin	3.46	79
N-Methylphenothiazine	3.44	72
Bis-(8-hydroxyquinolinato)copper(II)	3.2	72
NNN'N'-Tetramethyl-*p*-phenylenediamine	3.27	72
Carbazole*	3.44	80
NN-Dimethyldihydrophenazine**	3.22	81

*The crystal consists of domains in each of which the donor molecules are oriented in the same way[80].
**In the stack the donor and acceptor form a pair with an interplanar distance of 3.22 Å; the distance between the pairs is 3.54 Å.

The TCNQ–benzidine complex and its clathrate compounds with solvents consist of infinite stacks of alternating donor and acceptor molecules forming structures of three types. The first type, a complex without the solvent[83], consists of uniform stacks with an interplanar distance of 3.22 Å. The complex containing dichloromethane is made up to stacks in which the distance between the donor and acceptor is the same (3.22 Å) and the solvent molecules are accommodated in the channels between the stacks[84]. Complexes containing acetonitrile, acetone, and methylene chloride are constructed in exactly the same way. A third type of structure has been demonstrated for the complex containing benzene[85]. In this case the stacks consist of donor and acceptor dimers with an interplanar distance of 3.09 Å, benzene molecules being distributed in the channels between the stacks. Complexes containing toluene, nitrobenzene, and benzonitrile have similar structures.

TCNQ radical-ion salts are constructed differently. Since there are no fundamental differences between the structures of simple and complex TCNQ salts, we shall consider their structures by arranging the salts in groups based on different types of packing of anions.

Both simple and complex TCNQ salts consist in most cases of individual infinite stacks of anions. If the donor molecules are fairly planar, they can also form an infinite stack parallel to that of the acceptor. For spherical cations (for example, metal and ammonium cations), the donors are arranged in separate structures consisting of chains between the stacks of anions and parallel to the latter. Data for the structures of the TCNQ salts are

compiled in Table 7, in which the crystalline modification of the salt, the type of packing of the anions, the distance between neighbouring acceptor molecules, and the resistivity of the salt are indicated. The resistivity of TCNQ salt single crystals is minimal in the direction of the stack of anions and the anisotropy of the conductivity as a function of direction in the crystal can reach 10^4 (Table 6), so that the resistivity of the salt depends on the way in which the stack of anions is constructed.

The first group of salts have the highest resistivities (Table 7, compounds 1–5). The study of the structures of these salts showed that they do not contain stacks of anions at all, individual pairs or tetrads of anions separated by cations being present.

Table 7. The crystal structures of TCNQ radical-ion salts.

No.	Cation(donor)	Crystalline modification	Donor: acceptor	Structural formations	Distance between TCQD species, A	Refs.	Resistivity, Ω cm	Refs.
1	1,3-Dimethylbenzimidazole	Triclinic	1:1	Dimers	3.07	86	1.5×10^7	87
2	1,2,3-Trimethylbenzimidazole	Monoclinic	1:1	Dimers	3.12	88	1.4×10^9	87
3	3,3'-Diethylthiacyanine	Triclinic	1:1	Dimers	3.23	72	9×10^9	72
4	Dibenzenechromium	Monoclinic	1:1	Dimers	3.28	72	1.6×10^7	72
5	1,3,3'-Trimethyl-2-[*p*-(*N*-β-chloroethyl-*N*-methylamino)-styryl]indole	Monoclinic	1:2	Tetrads	w.t.[a]3.22 b.t.[b]3.45	72	–	–
6	Na	Triclinic	1:1	Stacks, two types of dimers	w.d.[c]3.22 w.d.[d]3.20 b.d.3.50 b.d.3.48	89	3×10^4	45
7	Rb-I (T = –190°C)	Monoclinic	1:1	Stacks, dimers	w.d.3.16	90	1×10^5	91
8	Ditoluene-chromium	Monoclinic	1:1	Stacks, dimers	w.d.3.33 b.d.3.42	72	2.5×10^5	72
9	Morpholinium	Triclinic	1:1	Stacks, dimers	w.d.3.28 b.d.3.61	92	1×10^2	45
10	3,3'-Dimethylthiocyanine	Monoclinic	1:2	Stacks, dimers	w.d.3.25 b.d.3.38	93	2.3×10^3	93
11	3,3'-Dimethylthiocarbocyanine	Monoclinic	1:2	Stacks, dimers	w.d.3.17 b.d.3.17	94	4.6×10^5	94
12	3,3'-Diethylthiocarbocyanine	Monoclinic	1:2	Stacks, dimers	w.d.3.24 b.d.3.24	95	6.6×10^3	95
		Triclinic	1:2	Tetrads	3.28	96	5×10^4	95
13	1,1'-Ethylene-2,2'-bipyridylium	Triclinic	1:2	Stacks, two types of dimers	w.d.3.22 w.d.3.26 b.d.3.59	97	1×10^3	97
14	*NN*-Dibenzyl-4,4'-bipyridylium	Triclinic	1:4	Stacks, tetrads	w.d.3.16 b.d.3.24 b.t.3.62	98	–	–
15	Triethylammonium	Triclinic	1:2	Stacks, dimers	w.d.3.22 b.d.3.30	99	0.3[e] 35; 7.2×10^2	99
16	Tetraphenylphosphonium	Monoclinic	1:2	Stacks, two types of dimers	w.d.3.12 w.d.3.21 b.d.3.35 b.d.3.49	72	4.5×10^3 1.7×10^6 2.1×10^6	72
17	Methyltriphenylarsonium	Triclinic	1:2	Stacks, tetrads	w.t.3.20 b.t.3.58	72	5.7×10^3 9×10^2 1×10^5	45
18	Methyltriphenylphosphonium ($T < 40$°C)	Triclinic	1:2	Stacks, tetrads	w.d.3.22 b.d.3.24 b.t.3.57	72	6×10^1 6×10^2 1×10^5	45
	$T > 40$°C	Triclinic	1:2	Stacks, tetrads	w.d.3.26 b.d.3.32 b.t.3.55	100	–	–
19	*N*-Propylquinolinium	Triclinic	1:2	Stacks, tetrads	w.d.3.24 b.d.3.28 b.t.3.43	101	0.5 6 4.5×10^2	45
20	3-Ethyl-1-methylbenzimidazolium	Triclinic	1:2	Stacks, two pairs of dimers	w.d.3.28 w.d.3.27 b.d.3.32	102	0.15 2.3×10^2 4.3×10^2	102
21	3-Ethyl-1,2-dimethylbenzimidazolium	Triclinic	1:2	Stacks, two pairs of dimers	w.d.3.21 w.d.3.27 b.d.3.38	103	15	103
22	Cs	Orthorhombic	2:3	Stacks, triads	w.t.3.22 b.t.3.26	72	1×10^3	72
23	Morpholinium	Monoclinic	2:3	Stacks, triads	w.t.3.25 b.t.3.24	104	5×10^3	45
24	Trimethylammonium	Monoclinic	2:3	Stacks, triads	w.t.3.26 b.t.5.15	105	–	–
25	K	Monoclinic	1:1	Stacks	3.40–3.50	72	1×10^4	45
26	Rb-II (T = 20°C)	Triclinic	1:1	Stacks	3.43	91	1×10^2	91
27	Ditoluenechromium	Triclinic	1:1	Stacks	3.29	72	0.5	72
28	*NNN'N'*-Tetramethyl-*p*-phenylenediamine	Triclinic	1:2	Stacks	3.24	72	–	–

[a] w.t. = within triad or tetrad. [b] b.t. = between triads or tetrads. [c] w.d. = within dimer. [d] b.d. = between dimers. [e] The resistivities of single crystals in three crystallographic directions are quoted.

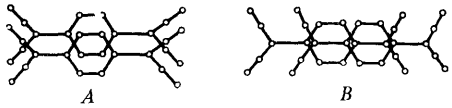


Figure 2.

The second most numerous group of salts (Table 7, compounds 6–24) contains inhomogeneous stacks of anions consisting of dimers, triads, or tetrads comprising the acceptor. The arrangement of neighbouring anions in the dimers is illustrated in Fig. 2*a*. In this arrangement the overlapping of the π orbitals of neighbouring molecules is optimal and in the majority of salts the arrangement of neighbouring anions in the dimers is of this type or similar. Examples of the arrangement of the anions in the stack between adjacent dimers are illustrated in Fig. 2*b*. The molecules are displaced along the long or short molecular axis relative to the optimal arrangement, which leads to an increase of the interplanar distance between neighbouring anions and this in turn leads to the variation of the resistivities of these salts from 10^5 to 1 Ω cm. In some cases, although the distance between the dimers is the same as that between the anions within the dimers (Table 7, compounds 11 and 12), the TCNQ molecules are displaced even more markedly than shown in Fig. 2*b* and there is almost no interaction between the dimers.

When the anions are grouped into tetrads, the latter usually consist of two dimers with optimal overlapping of the anions; the overlapping between pairs is as a rule intermediate between types (*a*) and (*b*) and that between tetrads is of type (*b*) or similar. There also exist tetrads in which the anions are distributed at the same distance, for example in the methyltriphenylarsonium salt of TCNQ.

It is noteworthy that formally complex salts should contain neutral TCNQ molecules. The study of the crystal structures of the salts and also comparison of the bond lengths and angles in the acceptor molecule showed that the charge in the complex salts is as a rule uniformly distributed between TCNQ and $TCNQ^0$, but this does not lead to the appearance of any new structural features in such salts. 2 : 3 Salts (Table 7, compounds 22–24), which have been combined into the second group, constitute an exception. Triads, in which the central acceptor molecule is neutral and two anions are present on either side of this molecule at the same distances have been detected in the structure of these salts. Since in many cases the accuracy of the determination of this structure is low, it is difficult to establish whether the stack contains neutral TCNQ molecules or whether the charge is distributed uniformly among all the acceptor molecules, so that this subgroup of salts may be much more extensive.

Uniform stacks of anions are characteristic of the third group of salts (Table 7, compounds 25–28); here the resistivity of the salt decreases with decrease of the distance between the anions. The third group includes also the structure of TCNQ salts, which exhibit a "metallic" temperature variation of the conductivity (the conductivity increases with decrease of temperature). In all these salts there is phase transition at a certain temperature and they are converted from an "organic one-dimensional metal" into a dielectric. Table 8 presents data for the structures of these salts, their conductivities, and their phase transition temperatures. Very short interplanar spacings in the stacks of anions and cations and correspondingly the highest conductivity known for organic compounds are characteristic of these salts.

Table 8. The crystal structures of TCNQ radical-ion salts with metallic type of conductivity.

Donor (cation)	Donor: acceptor	Distance between neighbouring species in stack		T_{trans}, K	$\sigma_{300\,K}$, Ω^{-1} cm^{-1}	References
		anions	cations			
Tetraselenofulvalene	1:1	*	*	40	800	106
Tetrathiofulvalene	1:1	3.17	3.47	58	600	107
Tetrathiotetracene	1:2	3.18	3.52	90	20—160	108
N-Methylphenazinium	1:1	3.26	3.36	200	140	109
Quinolinium	1:2	3.22	3.50	240	100	109
Acridinium	1:2	3.25	3.42	150	—	109

*According to preliminary data [106], the structure of the TSF–TCNQ complex is very close to that of the TTF–TCNQ complex.

Salts with infinite stacks of anions, each of which contains a free electron, may be regarded as quasi-one-dimensional metals; we shall return to the properties of these systems in discussing the electrical and magnetic properties of TCNQ complexes.

2. Spectroscopic Properties

As mentioned above, the electronic absorption spectra of TCNQ molecular complexes contain, apart from the absorption bands of the donor and acceptor, also a charge-transfer band (TCB). The appearance of the latter is a characteristic feature of the formation of complexes and spectroscopic evidence for the formation of complexes with TCNQ is frequently used [67,110–113]. Table 9 indicates the positions of the charge-transfer bands for a number of TCNQ molecular complexes with various aromatic donors. Evidently the position of this band can vary within very wide limits.

With increase of the strength of the donor (with decrease of its ionisation potential), TCNQ complexes become increasingly more ionic and in the case of a radical-ion salt an overall spectrum of the donor and acceptor ions is observed. The spectra of complexes of intermediate strength [stability?] contain bands due to the donor cation and the $TCNQ^-$ anion in addition to those of the donor and acceptor and the charge-transfer band. This was clearly demonstrated in a study of the electronic absorption spectra of complexes of a single donor with a series of acceptors. Thus,1,6-diaminopyrene forms molecular complexes with chloranil, bromanil, and iodanil, while TCNQ gives rise to radical-ion salts [118]. Similar results were obtained for a series of complexes of poly-(*p*-dimethylaminostyrene) [119].

Table 9. The positions of the charge-transfer band in the spectra of TCNQ complexes.

Donor	λ_{max}, nm	Solvent*	Refs.	Donor	λ_{max}, nm	Solvent*	Refs.
Hexamethylbenzene	595	A	47	*NN*-Di-n-butylaniline	940	A	28
Pentamethylbenzene	540	B	113	*p*-Toluidine	820	C	116
Biphenyl	510	A	47	*NN*-Dimethyl-*p*-toluidine	830	A	28
trans-Stilbene	635	A	47	4-Bromo-*NN*-dimethylaniline	755	A	28
Naphthalene	588	A	47	Diphenylamine	885	C	116
Anthracene	823	A	47	Triphenylamine	960	C	116
Phenanthrene	535	A	114	1-Naphthylamine	788	A	47
Pyrene	763	A	47	*NN*-Dimethyl-1-naphthylamine	800	A	28
Naphthacene	1040	A	47	*NN*-Dimethyl-2-naphthylamine	820	A	28
1,2-Benzopyrene	610	B	112	Indole	625	A	47
3,4-Benzopyrene	862	A	47	Catechol	540	A	47
Perylene	950	A	47	Anisole	530	A	28
3-Methylchloranthrene	925	A	47	Phenetole	545	A	28
Fluorene	607	B	114	Veratrol	583	A	28
Phenoxazine	820	A	115	2-Naphthol	653	A	47
Phenoxazine	1160	A	115	4-Aminoazobenzene	740	A	56
Phenothiazine	1200	A	115	4-Dimethylaminoazobenzene	950	A	56
N-Methylphenothiazine	1250	A	115	4-Dimethylamino-4'-methylthioazobenzene	970	A	56
1,2-Benzofluorene	635	B	116	4-Diethylaminoazobenzene	875	A	56
Carbazole	578	B	114	4-Ethyl-4'-diethylaminoazobenzene	1000	A	56
Thiophen	480	A	28	*p*-Phenylenediamine	628	C	116
Dibenzothiophen	526	B	114		875		
Dibenzofuran	510	B	114	*m*-Phenylenediamine	840	C	116
Chrysene	628	B	47	*NNN'N'*-Tetramethyl-*p*-phenylenediamine	620	C	116
					1055		
Coronene	740	A	47		1163	B	117
Triphenylene	575	A	47	2,3,5,6-Tetramethyl-*p*-phenylenediamine	630	C	116
					875		
p-Terphenyl	598	A	47	Benzidine	535	C	116
					1020		
Aniline	736	C	116	*NNN'N'*-Tetramethylbenzidine	550	C	116
					1285		
N-Methylaniline	752	A	47	Di-(4-aminophenyl)amine	610	C	116
N-Ethylaniline	758	A	47		875		
Acetanilide	550	A	28		1110		
N-Methylacetanilide	590	A	28				
NN-Dimethylaniline	835	C	116				
NN-Diethylaniline	880	A	–				
NN-Di-n-propylaniline	920	A	28				

*A = chloroform, B = methylene chloride, and C = polycrystalline film.

A very large number of studies have been made on the spectra of TCNQ radical-ion salts. It was established initially that the $TCNQ^-$ radical-anion in acetonitrile solution has a fairly complex spectrum, consisting of two main bands with λ_{max} = 420 nm (ϵ = 24 300) and 842 nm (ϵ = 43 300) and several weak bands with λ_{max} = 665, 680, 744, and 760 nm. [45] It follows from these results that the intensity ratio of the bands with λ_{max} = 420 and 842 nm for simple TCNQ radical-ion salts is 0.5, which is one of the main characteristics of simple TCNQ salts. For comparison, one may point out that the absorption spectrum of the 11,11,12,12-tetracyano-2,6-naphthoquinodimethane radical-anion has bands with λ_{max} = 1105 nm (ϵ = 66 200), 938 nm (ϵ = 23 500), 838 nm (ϵ = 5800), 518 nm (ϵ = 12 600), and 418 nm (ϵ = 25 500). [2]

In aqueous solutions the $TCNQ^-$ radical-anion forms dimers, which has been established in a spectrophotometric study of solutions of the lithium salt of TCNQ in water.

In other solvents (methylformamide, methanol, acetonitrile) dimerisation was not observed. The dimer has an absorption band with $\lambda max = 643$ nm.[120] The equilibrium constant for the dimerisation reaction $2\,TCNQ^- \rightleftharpoons (TCNQ)_2^{2-}$ proved to be 1.2×10^4 litre mole^{-1} at 14°C.[121]

Table 10. The parameters of the reflection spectra of simple (Nos. 1–16) and complex (Nos. 17–24) TCNQ radical-ion salts.

No.	Salt	λ_{max} for different bands, nm			Refs.
		α	β	CTB	
1	Li^+-$TCNQ^-$	364	617	1280	122
2	Na^+-$TCNQ^-$	364	613	1075	122
3	K^+-$TCNQ^-$	360	610	1180	122
4	NH_4^+-$TCNQ^-$	376	655	970	122
5	$Ph_3(Me)P^+$-$TCNQ^-$	375	655	970	122
6	Rb^+-$TCNQ^-$-I	369	635	1030	123
7	Ni^{2+}-$(TCNQ^-)_2$	395; 375	635	1110	123
8	Fe^{2+}-$(TCNQ^-)_2$	392; 372	650	1165; 950	123
9	Co^{2+}-$(TCNQ^-)_2$	400; 376	650	1135; 950	123
10	Mn^{2+}-$(TCNQ^-)_2$	400; 388	655	1110	123
11	Rb^+-$TCNQ^-$-II	356	600	1350	123
12	Cs^+-$TCNQ^-$	364	715; 625	1390;1075	123
13	Ba^{2+}-$(TCNQ^-)_2$	382	725; 650	1000	123
14	Morpholinium$^+$-$TCNQ^-$	362	615	1050	122
15	*N*-Methylphenazinium$^+$-$TCNQ^-$	388	620	850	122
16	*N*-Methylquinolinium$^+$-$TCNQ^-$	395	675		122
17	Cs_2^+-$(TCNQ)_3^{2-}$	364	617	990	131
18	(Morpholinium$^+$)$_2$-$(TCNQ)_3^{2-}$	364	614	1000	131
19	$Ph_3(Me)P^+$-$(TCNQ)_2^-$	380	585	962; 877	131
20	$Me_3(Ph)N^+$-$(TCNQ)_2^-$	380	610	980; 870	131
21	Et_3NH^+-$(TCNQ)_2^-$	368	610	972; 887	131
22	Quinolinium$^+$-$(TCNQ)_2^-$	375	575	953	131
23	*N*-Methylacridinium$^+$-$(TCNQ)_2^-$	364	562	895	131
24	*N*-Methylquinolinium$^+$-$(TCNQ)_2^-$	375	575	887; 980	131

The study of the reflection spectra of crystalline simple radical-ion TCNQ salts showed that they differ appreciably from those of the solutions. The reflection spectrum contains three types of lines, designated as the α, β, and charge-transfer lines. Data for some complexes are presented in Table 10 (compounds 1–16). Some investigators regard the α and β bands as the absorption bands of the monomeric TCNQ anions[124,125] which have been strongly displaced relative to their positions in the spectrum of the solutions (420 and 842 nm in acetonitrile), while others regard them as the absorption bands of $TCNQ^-$ dimers (380 and 647 nm in water)[120–130]. The charge-transfer band has been assigned to charge transfer between $TCNQ^-$ anions.

A more thorough recent study of the reflection spectra of simple TCNQ salts and comparison of the spectra with the crystal structure of the salts make it possible to divide the salts into three groups[123]. For the first group of salts, the α and β bands are probably those of the dimers (Table 10, compounds 1–10). The second group occupies an intermediate position. For the third group, the α and β bands are more likely to be those of monomeric $TCNQ^-$ anions which have been strongly displaced (compounds 13 and 14). Although new data for the structure of TCNQ salts (for example Refs. 89–92) throw doubt on the validity of the assignment of the individual salts to a particular group, the overall approach appears to be extremely promising for the elucidation of the dependence of the spectroscopic properties of TCNQ salts on their structure and also for the investigation of the nature of the interaction between the anions in the columns.

The study of the reflection spectra of complex crystalline TCNQ salts showed that they too contain three types of bands (Table 10, compounds 17–24)[131]. Those of highly conducting complex salts show only one explicit electronic absorption band in the range 2000–3500 nm. It has been suggested that this is a band corresponding to charge transfer between neutral TCNQ and its radical-anion[129].

The study of the mirror reflection spectra of single crystals of two complex TCNQ salts with triethylamine and 3,3′-diethylthiocarbocyanine in polarised light showed that the charge-transfer band as well as a band at longer wavelengths are polarised in the direction of the chains of $TCNQ^-$ anions and are due to electron transfer between two $TCNQ^-$ radical-anions (the first band)[127] and between a radical-anion and a neutral TCNQ molecule (the second band)[127].

A bathochromic shift of the α and β bands was observed in a study of the electronic spectra of the lithium and potassium radical-ion salts at a high pressure, which was explained by a shift of the equilibrium between the monomeric and dimeric forms of the $TCNQ^-$ anions[132]. A similar bathochromic shift was observed also for the charge-transfer band[133] owing to the decrease of the distance between the $TCNQ^-$ anions on compression. It was found that the effect of the magnetic field is similar to that of the solvent on the absorption spectra of salts on passing from a non-polar to a polar solvent[134].

The study of the infrared spectra of the TCNQ complexes and radical-ion salts showed that the spectrum of acceptor, both neutral[135] and anionic[136,137], persists in both cases. The $TCNQ^-$ vibrations differ from those of TCNQ by a comparatively slight frequency shift. The frequency of the C≡N vibrations shifts by 25–30 cm^{-1} towards lower values, which is characteristic of all TCNQ salts and the band itself usually splits into 3–4 components, separated from one another by 10–15 cm^{-1}. The type B_{2u} and B_{3u} C=C vibration frequencies differ from one another much more markedly than for TCNQ: 1515 and 1590 cm^{-1} instead of 1540 and 1545 cm^{-1}.[127] A broadening of the bands in the range 1100–1600 cm^{-1} is characteristic of highly conducting TCNQ salts and the half-width of the bands can reach 150 cm^{-1}.[137] A study of the infrared spectra of the complexes and the radical-ion salts in the range 20–400 cm^{-1} showed that there is an absorption head in the region of 40 cm^{-1}, interpreted as corresponding to direct allowed transitions from the ground to the excited band, which is probably also the conductivity band[138].

It is noteworthy that molecular vibrations which are forbidden in free molecules can frequently become allowed in charge-transfer complexes. Thus the band (1565 cm^{-1}) due to the stretching vibrations of the C=C bond in TCNQ becomes allowed in the 1:1 TCNQ–hexamethylbenzene complex and the band (1296 cm^{-1}) due to the stretching vibrations of the C–CH_3 bonds of hexamethylbenzene appears in the spectrum of the 1:2 complex[135].

The use of NMR for the investigation of TCNQ complexes is of interest. Thus, by measuring the chemical shift of the hexamethylbenzene protons in the complex with TCNQ relative to the positions of the signals for the pure donor, it was possible to determine the equilibrium constant for this complex[139]. An NMR study of highly conducting TCNQ salts[140,141] demonstrated the localised nature of the electronic states in the salts at low temperatures.

3. Electrical and Magnetic Properties

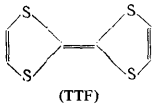
TCNQ complexes as well as the complexes of other well known acceptors as a rule exhibit semiconducting properties. The temperature variation of their conductivity can be described by the equation

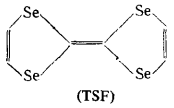
$$\sigma = \sigma_0 e^{-\epsilon/kT},$$

where σ is the conductivity at a given temperature T (on the absolute scale), σ_0 a number characterising the conductivity of $T = \infty$, k the Boltzmann constant, and ϵ the thermal activation energy.

The first studies on TCNQ complexes were in fact devoted to the investigation of the electrical properties of these compounds [142,143]. Most of the data published since that time have been summarised in the monograph of Gutmann and Lyons [144], where the properties of TCNQ complexes are discussed among those of other organic semiconductors. The electrical properties of TCNQ complexes are also discussed in two other reviews, one of which is likewise devoted to organic semiconductors [145] and the other deals with the problem of high-temperature superconductivity [146].

The resistivities of TCNQ complexes were quoted previously in Tables 2, 4, 5, 7, and 8. The TCNQ complexes of tetrathiofulvalene (TTF), [107] *trans*-*cis*-dimethyl-TTF, [147] tetramethyl-TTF, [148] and tetraselenofulvalene (TSF) [106] exhibit the highest conductivities.


(TTF)


(TSF)

While the mechanism of conduction by TCNQ complexes with high resistivities has been fairly thoroughly investigated [144] (these complexes differ little from those of other widely used acceptors), the elucidation of the mechanism of conduction in highly conducting TCNQ salts is at present the most interesting task (salts with "metallic conductivity" will be discussed separately).

Hitherto most studies have dealt with the synthesis of new TCNQ complexes [49,62,63,66,147-150], which are as a rule characterised by their conductivities. At the same time more thorough studies are being made of the electrical properties of TCNQ complexes synthesised previously. Thus two activation energies (for temperatures below and above 400 K) have been obtained from the temperature variation of the conductivity of single crystals of simple alkali metal salts of TCNQ in the temperature range 300 to 540 K. A change from hole to electronic conductivity was observed for the sodium and potassium salts when the activation energy changed [151], which clearly indicates the occurrence of two conduction mechanisms in these salts. A first-order phase transition in the range 350–400 K was recently observed [152] for the same salts, which may be associated with the change in the activation energy for conduction. A more complex change in activation energy was found for the triethylammonium$^+$-$(TCNQ)_2^-$ salt [153,154]; here the activation energies pass through a maximum at 222 K. The activation energies for conduction, determined for different crystallographic directions in single crystals of triphenylmethylphosphonium$^+$-$(TCNQ)_2^-$ [155,156] and triphenylmethylarsonium$^+$-$(TCNQ)_2^-$ [157] also differ.

Thus the activation energy may depend on the temperature and the direction of motion of the carriers, which is probably associated with a more complex mechanism of conduction than in the usual semiconductors. Studies on the changes in conductivity and in activation energy for conduction in TCNQ salts as a function of pressure are of interest from this standpoint [158-160]. As a rule the conductivity increases with increase of pressure, while the activation energy falls.

It is significant that, even at the highest pressures, metallic conductivity was not observed in the salts [159], i.e. the overall variation of the conductivity with temperature remained characteristic of semiconductors.

In order to investigate the conduction mechanism, it is important to determine the type of charge carriers and their mobility. However, the mobilities found in measurements of the Hall effect for single crystals of a number of highly conducting TCNQ salts [161-163] are low (0.6 to 0.004 $cm^2 V^{-1} s^{-1}$) and do not permit preference to be given to any one conduction mechanism.

The thermo-e.m.f.'s of a number of TCNQ salts have been measured [161,164,165]. The sign of the thermo-e.m.f. of highly conducting quinolinium, acridinium, and *N*-methylphenazinium salts indicates electronic conductivity, while that of the complex triethylammonium salt indicates hole conductivity. It is therefore impossible to reach unambiguous conclusions concerning the mechanism of conduction in TCNQ salts with low resistivities. Whereas some investigators discuss the observed conductivities and activation energies within the framework of the band model [153], others postulate a jump mechanism [165,166]. The latter is probably preferable, since the majority of data indicate the presence of a system of localised current carriers, the motion of which at any stage must include a thermally activated jump. At least the low-temperature conductivities of a number of highly conducting TCNQ salts are described satisfactorily by this model [167-170].

It is noteworthy that the discrepancy between the electrical properties of TCNQ complexes, frequently found in studies by different investigators, can be accounted for by the lack of purity criteria for these compounds. Thus the *N*-methylphenazinium salt of TCNQ synthesised from highly pure components, exhibits a higher conductivity at an elevated temperature than stated previously and at low temperatures (below 100 K) its conductivity is ten times lower than that described in an earlier investigation [171]. Another cause is a marked influence of gaseous impurities, which may play a significant role in measurements on polycrystalline specimens. Thus, when simple alkali metal radical-ion salts are heated *in vacuo*, the conductivity falls, the activation energy for conduction increases, and the thermo-e.m.f. changes sign [161,172], which can be explained by the influence of atmospheric oxygen, playing the role of an electron-accepting impurity.

The magnetic properties of TCNQ complexes are also being vigorously investigated. Although molecular complexes and simple radical-ion salts are as a rule diamagnetic, the complex salts are paramagnetic. A qualitative correlation may be traced between the concentration of unpaired spins and the conductivity of TCNQ complexes (Table 11). [112]

The presence of an ESR signal of TCNQ complexes indicates a radical-ion nature of the complex, a phenomenon which is frequently used to determine the type of intermolecular bond (i.e. whether the given substance is a molecular complex or a radical-ion salt) [173,174].

The study of the ESR spectra of a large number of radical-ion salts [175-180] showed that complex TCNQ salts give rise to a fairly intense ESR signal; the number of unpaired spins per complex molecule varies from 1.5 to 10^{-2}. For simple salts, the concentration of free spins is much lower, which can be explained by the very strong

pair interaction between ions of the same kind. On the other hand, in the crystal lattices of highly conducting TCNQ salts the ions form infinite stacks with the same interionic distances; such salts as a rule give rise to an intense ESR signal. Complex salts with a low conductivity have a weak ESR signal for the same reasons as in the case of simple TCNQ salts.

Table 11. The number of unpaired spins per donor–acceptor pair in TCNQ complexes.

Complex	Number of unpaired spins per complex molecule	Conductivity at 300 K, Ω^{-1} cm^{-1}
N-Methyl-2,3-benzoquinolinium$^+$-$(TCNQ)_2^-$	1.3	2.8×10^{-2}
N-Methyl-3,4-benzoquinolinium$^+$-$(TCNQ)_2^-$	0.05	4.3×10^{-3}
N-Methyl-7,8-benzoquinolinium$^+$-$(TCNQ)_2^-$	0.056	8.0×10^{-3}
Hexamethylbenzene-TCNQ: single crystal	7.5×10^{-4}	–
polycrystalline powder	1.8×10^{-3}	–
1,2-Benzopyrene-TCNQ: single crystal	4.0×10^{-5}	–
polycrystalline powder	1.8×10^{-3}	1.9×10^{-12}
3,4-Benzopyrene-TCNQ: polycrystalline powder	6.3×10^{-4}	2.4×10^{-11}

TCNQ complexes with benzidine, which form clathrate compounds with solvents[51], constitute an interesting example of the mechanical generation of spins. The crystals of the complex are not paramagnetic both in the presence and absence of a solvent. However, when the crystals of a complex containing the solvent are ground to a powder, a strong ESR signal ($g = 2.0027$) is observed.

A careful study of the ESR spectra of various TCNQ salts over a wide range of temperatures showed that the behaviour of one set of triplets in the spectra is independent of temperature and is due to impurities and defects in the crystal lattice. Those in another set represent thermally excited triplet states, the concentration of which depends on temperature[181,182]. Similar results were obtained in a study of the dynamics of the nuclear polarisation of protons in simple alkali metal salts of TCNQ[183] and in the complex triphenylmethylarsonium salt of TCNQ.[184] Triplets of a new type, existing in the temperature range from 4 to 80 K, were observed in the ESR spectrum of the latter salt[182]. The authors suggest that this triplet is formed by two unpaired electrons delocalised over the neighbouring chains of $TCNQ^-$ anions.

The occurrence of a phase transition in the triphenylmethylphosphonium$^+$-$(TCNQ)_2^-$ and triphenylmethylarsonium$^+$-$(TCNQ)_2^-$ salts was confirmed with the aid of ESR.[185]

The method of double electron–electron resonance has been used recently to investigate triplet states[186,187]. The study by this method of the triplet excitons in TCNQ ion-radical salts of triphenylmethylphosphonium and cyanine dyes in the temperature range 150–350 K demonstrated that the formation of triplets is an activated process.

The temperature variation of the magnetic susceptibilities of simple[188,189] and complex[190] TCNQ salts and of salts with high[191] and moderate[192,193] conductivities has been studied. Whereas at high temperatures the magnetic susceptibility may increase slightly or fall with decrease of temperature, it increases sharply starting from 50 K. The low-temperature increase of suceptibility is not associated with the presence of paramagnetic impurities and reflects the intrinsic properties of the complexes.

We may note that the magnetic properties of TCNQ salts, as well as their electrical properties, depend on their structures. Thus, when the highly conducting ($\sigma = 380\ \Omega^{-1}$ cm^{-1}) *N*-methylphenazinium salt of TCNQ, which gives rise to a strong ESR signal, was recrystallised, a non-magnetic phase with $\sigma = 7.67 \times 10^{-5}\ \Omega^{-1}$ cm^{-1}) was obtained; by crystallisation, it can be reconverted into the initial form[194].

Yet another aspect of studies of the electrical properties of TCNQ complexes should be noted. In 1964 Little suggested[195,196] the possibility of an exciton mechanism of superconductivity in which there is attraction between conductivity electrons owing to exciton exchange (electronic excitations) and not phonon exchange. According to certain estimates, an exciton mechanism should lead to much higher temperatures of the superconductivity transition (above 300 K).

The manifestation of an exciton superconductivity mechanism requires a certain combination of two subsystems: one conducting and another dielectric with the appropriate exciton spectrum. Complex radical-ion salts proved to be promising for the synthesis of systems satisfying the requirements of Little'e model, since infinite stacks of anions in the highly conducting salts are effective conducting systems and polarisable cations can constitute dielectric systems. TCNQ salts of dyes were in fact synthesised for this purpose[58,59,197,198]. These salts did not exhibit superconductivity, but behaved as typical organic semiconductors; this was readily accounted for after the investigation of their crystal structure which does not contain infinite uniform stacks of TCNQ anions.

A sensational report of an extremely high conductivity of the TCNQ–tetrathiofulvalene (TTF) complex (10^6 Ω^{-1} cm^{-1}), observed at 60 K, appeared recently; on cooling from 300 to 60 K the conductivity, being of the metallic type, increased by a factor of 500.[199] The authors regarded this conductivity as a result of fluctuations leading to temporary transitions to the superconducting state of the complex near the structural transition temperature. This report led immediately to vigorous studies on this compound. Repeated measurements of the conductivity of the complex, carried out by different investigators[200–202], including measurements by the contactless method at high frequencies, failed to confirm such a high increase of conductivity; at 60 K it increases by a factor of 10 to 150, probably depending on the purity of the test specimen.

Conductivity of the metallic type has now been observed for a fairly large set of TCNQ complexes (Table 8), which can be divided into two groups. A low phase transition temperature (<100 K), a symmetrical cation, and a high conductivity are characteristic of the first group (complexes with tetraselenofulvalene, tetrathiofulvalene, and tetrathiotetracene). In this group the TTF–TCNQ complex has been investigated in greatest detail; using it, we shall trace the changes in the properties of such complexes as a function of temperature.

The study of the crystal structure of the TTF–TCNQ complex at room temperature showed that, as for all highly conducting TCNQ salts, infinite columns of anions and cations with interplanar distances of 3.17 Å between neighbouring anions and 3.47 Å between neighbouring cations are characteristic of this complex[107]. At 40 K the structure of the complex remains unchanged and there is only a slight decrease of the distances between the neighbouring anions and cations, to 3.11 and 3.43 Å respectively[203].

In terms of the variation of its thermo-e.m.f., the TTF–TCNQ complex behaves as a metal in the temperature range from 140 to 56 K; at 56 K the Seebeck coefficient becomes abruptly zero, changing sign at lower temperatures[204].

The study of the magnetic properties of the complex showed[205] that the substance is diamagnetic at $T < 20$ K and paramagnetic at $T > 20$ K, the magnetic susceptibility increasing monotonically with increase of temperature to 359 K. The spectroscopic properties of the TTF–TCNQ complex have been investigated: the polarisation absorption spectra[206] and the reflection spectra of single crystals[207]. The overall form of the spectrum is typical for TCNQ radical-ion salts. A plasma absorption head was observed at 1.4 μm. The transition to the dielectric state below 60 K was confirmed also by heat capacity measurements[208]. On the basis of all the above findings, it is suggested that a metal–dielectric transition of the pyerls (structural) type probably occurs in this group of salts[209].

The second group includes the simple *N*-methylphenazinium salt of TCNQ and the complex quinolinium$^+$-$(TCNQ)_2^-$ and acridinium$^+$-$(TCNQ)_2^-$ salts. A comparatively high-temperature metal–dielectric transition has been observed (from conductivity measurements; below the transition temperature the conductivity is of the semiconductor type) for these salts, which contain asymmetric cations. The study of other properties of the salts—magnetic susceptibility[210], heat capacity[211], and optical properties[212]—demonstrated the occurrence of a phase transition at 14 K for the quinolinium$^+$-$(TCNQ)_2^-$ salt and in the region of 10–30 K for the *N*-methylphenazinium salt of TCNQ. It is suggested that at low temperatures (<~15 K) these salts are in the state of a disordered Mott–Hubbard dielectric, which behaves as a one-dimensional disordered metal above the phase transition temperature (~15–~200 K).[212] The non-metallic type of temperature variation in this temperature range may be associated with the spatial localisation of electrons, arising owing to the disorder in the crystal lattice, which in turn can be accounted for by the asymmetry of the cations[210].

Although all known TCNQ salts with the metallic type of conductivity are converted into dielectrics at a low temperature, the question of the possible superconductivity of these compounds (for example, near the phase transition temperature) still remains unresolved. The instability of such quasi-one-dimensional electronic systems had been demonstrated theoretically before the systems were obtained experimentally[209] and further studies on these salts should show whether or not they are capable of superconductivity. Furthermore, these salts constitute an excellent model of a quasi-one-dimensional metal and the study of such systems is extremely interesting from the standpoint of solid state physics.

In connection with this problem, mention may be made of several other investigations. It has been shown that organic compounds, including TCNQ, influence the temperature of the transition to the superconducting state in thin metallic films[213]. Thus TCNQ sputtered onto a thin vanadium film (50–200 Å) reduced the temperature of its transition to the superconducting state, while electron-donating compounds, for example anthracene, increased it by 0.05–0.1 K. The material obtained by the simultaneous sputtering of aluminium and TCNQ behaves similarly[214].

In conclusion mention should be made of studies undertaken to create conducting polymeric materials. Using various polymeric molecules as electron donors, TCNQ complexes and radical-ion salts have been obtained. A large number of materials of this type have been patented[215–222], their resistivities amounting to 100–1000 Ω cm. Another method for the synthesis of conducting materials involves the addition of the lithium salt of TCNQ to a polymer containing amino-groups. Whereas the initial polymers have resistivities of about 10^{16} Ω cm, the materials obtained by this procedure have a resistivity of about 10^8 Ω cm, although the amount of added salt does not exceed 5%.[223–225].

A review published recently[226] is devoted to complexes of polymeric donors with various acceptors, including TCNQ. We shall merely mention that the polymeric complexes have still been very little investigated and a large field of research awaits investigators in this connection. The electrical[227–230] and magnetic[231] properties of polymeric TCNQ complexes are being mainly studied at the present time. The first attempts are being made to relate the electrical properties of the complexes to their structures[232]. If TCNQ complexes do find applications, they are most likely to be complexes based on polymeric donors.

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We have examined the principal aspects of research on TCNQ carried on at the present time. The study of reactions of TCNQ with nucleophilic agents, via intermediate one-electron oxidation, is the most interesting and promising in the chemical sense; such organic reactions have so far been inadequately investigated. The stable $TCNQ^-$ radical-anion is also an interesting object of study in reactions with radical and electrophilic reagents.

The electrical properties of TCNQ complexes have been primarily investigated in studies on the properties of crystals with conductivity of the metallic type. The problem of the possible superconductivity of such systems is extremely important. Crystals of this kind are also interesting from the standpoint of the physical properties of a quasi-one-dimensional electronic system.

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Advances in the Chemistry of Aliphatic Diazosulphones

A.L.Fridman, Yu.S.Andreichikov, V.L.Gein, and S.S.Novikov

Methods for the synthesis of α-diazosulphones are examined and a systematic account is given of the literature data on the physicochemical properties and ultraviolet, infrared, and NMR spectroscopy of this interesting class of aliphatic diazo-compounds. Much attention is devoted to chemical reactions of α-diazosulphones via the intermediate formation of carbonium ions and sulphonyl carbenes as well as reactions involving the nitrogen of the diazo-group. In many cases a comparative description is given of the chemical properties of α-diazosulphones and α-diazoketones. The review constitutes the first compilation of the chemistry of α-diazosulphones available in the literature.
The bibliography includes 76 references.

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I. INTRODUCTION

A number of interesting reviews have been published recently on the chemistry of aliphatic diazo-compounds[1-8], dealing mainly with methods of synthesis, properties, and structures of diazoalkanes or diazocarbonyl compounds, but the chemistry of α-diazosulphones has not been considered. Nevertheless this class of aliphatic diazo-compounds has been attracting attention because of the presence in the molecule of both the sulphonyl and diazo-groups. The combination of these groups makes it possible to synthesise new types of sulphones, whose preparation by other procedures is difficult. Furthermore, α-diazosulphones are of theoretical interest as regards the comparison of their reactivities with those of α-diazoketones, diazophosphines, and silyldiazoalkanes.

The first diazosulphonyl compound—potassium diazomethionate—was synthesised by Pechmann and Mank in 1895.[9] After that not a single new method of synthesis of α-diazosulphones and not a single new compound of this class were described until 1962.

A fruitful stage in the chemistry of α-diazosulphones began in 1962, when the Dutch chemists Strating and Lensen[10] described a method for the preparation of monosulphonyldiazomethanes and the German investigators Klages and Bott[11] published a report on bis-(phenylsulphonyl)diazomethane. Subsequent advances in the synthesis of diazosulphones (of which about 50 are now known) stimulated an increase of interest in the structure and properties of these compounds.

The aim of the present review is to give a systematic account of the literature data on the methods of synthesis, structures, and chemical properties of diazosulphones.

II. METHODS OF SYNTHESIS

The classical method of synthesis of α-diazoketones[12] by the interaction of carboxylic acid chlorides with an excess of diazomethane,

$$RCOCl \xrightarrow{CH_2N_2} RCOCHN_2 + CH_2Cl + N_2 ,$$

leads to positive results only in the case of toluene-*p*-sulphonyl chloride[13], which give rise in this reaction to tolylsulphonyldiazomethane and α-chloro-α-tolylsulphonylmethane:

$$CH_3C_6H_4SO_2Cl \xrightarrow{CH_2N_2} CH_3C_6H_4SO_2CHN_2 + CH_3C_6H_4SO_2CH_2CH_2Cl.$$

The interaction with 2-phenylethanesulphonyl chloride takes place in the presence of base via the intermediate 2-phenylthioacetaldehyde *SS*-dioxide to give benzylethylene sulphone[14]:

$$C_6H_5CH_2CH_2SO_2Cl \xrightarrow{CH_2N_2} \begin{cases} \not\rightarrow\ C_6H_5CH_2CHSO_2CH_2N_2 \\ \rightarrow\ [C_6H_5CH_2CH{=}SO_2] + C_6H_5CH_2CH{-}CH_2 \\ \qquad\qquad\qquad\qquad\qquad\qquad\quad SO_2 \end{cases}$$

α-Diazosulphone is not formed under these conditions[15]. Evidently diazomethane is incapable of attacking the sulphur atom in view of its inadequate electrophilic properties. This is why α-diazosulphones, with the exception of potassium diazomethionate, remained unknown for a long time.

It is noteworthy that the synthesis of α-phenyl-α-(*p*-toylsulphonyl)diazomethane from toluene-*p*-sulphonyl chloride and phenyldiazomethane is described in one of the latest communications[16]:

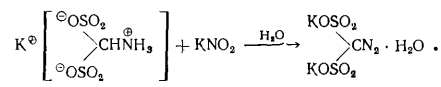
$$CH_3C_6H_4SO_2Cl + C_6H_5CHN_2 \xrightarrow{-HCl} CH_3C_6H_4SO_2\overset{C_6H_5}{\underset{|}{C}}N_2 .$$

We believe that this procedure for the preparation of α-diazosulphones requires a detailed study, since it has been described for only one example and the diazo-derivative was not isolated in a pure form.

The main methods for the synthesis of α-diazosulphones were developed in the 1960s. They include the oxidation of the hydrazones of disulphonylketones, the introduction of the diazo-group into an activated methylene group with the aid of tosyl azide, and the alkaline cleavage of *N*-nitrosourethanes and α-diazo-β-oxosulphones. The above methods are not equivalent as regards ease, universality, and simplicity. However, considered together, they make it possible to obtain α-diazosulphones with various substituents.

1. Diazotisation of Aminomethionic Acid Salts

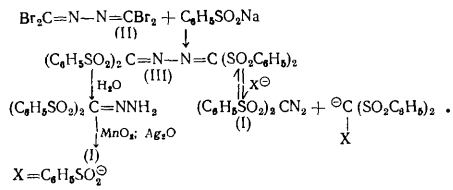
The method consists of the diazotisation of potassium aminomethionate[9] (or the sodium salt[17]) with nitrite ions at an elevated temperature:



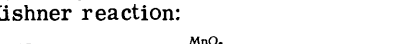
It has been described only for two compounds. However, one cannot rule out the possibility that it can be used to diazotise other derivatives of aminomethionic acids.

2. Oxidation of Bis(arenesulphonyl)formaldehyde Hydrazone

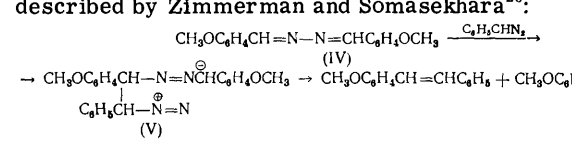
The method has been developed for the synthesis of bis(benzenesulphonyl)diazomethane (I).[18,19] It is obtained from carbonyl bromide azine (II) and sodium benzenesulphinate:



The bis(benzenesulphonyl)formaldehyde azine (III) formed in the first stage is hydrolysed to the corresponding hydrazone, which is oxidised with activated manganese dioxide or silver oxide to bis(benzenesulphonyl)diazomethane. Bis(benzenesulphonyl)methane is isolated as a side product, being formed according to the authors via the Wolff–Kishner reaction:



The interaction of the azine (II) with sodium benzenesulphinate in the absence of moisture and subsequent treatment of the reaction mixture with alumina also make it possible to obtain a high yield of the diazosulphone (I). The intermediate azine (III) probably reacts readily with the nucleophilic agent ($X^{\ominus}$) present in the reaction mixture. A similar base-catalysed decomposition of *p*-methoxybenzylideneazine (IV) by phenyldiazomethane has been described by Zimmerman and Somasekhara[20]:

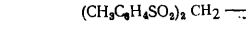


In this case phenyldiazomethane attacks the azine (IV). The resulting unstable intermediate adduct (V) decomposes into 1-(*p*-methoxyphenyl)-2-phenylethylene and *p*-methoxyphenyldiazomethane with evolution of nitrogen.

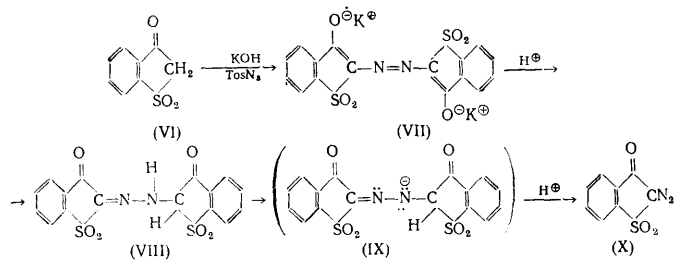
It is noteworthy that the above method of synthesis of α-diazo-β-disulphones can probably by used also to prepare substituted bis(arenesulphonyl)diazomethanes, but the initial bis(arenesulphonyl)formaldehyde hydrazones are difficult to obtain.

3. The Reactions of Tosyl Azide with Compounds Containing an Activated Methylene Group

The method was described in 1964 for the synthesis of bis(arenesulphonyl)- and bis(alkanesulphonyl)-diazomethanes[21]. Thus bis(toluene-*p*-sulphonyl)diazomethane is obtained by treating an aqueous alcoholic solution of bis(toluene-*p*-sulphonyl)methane and sodium hydroxide with an ethereal solution of tosyl azide:

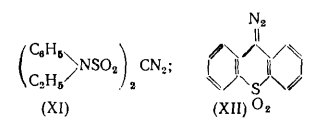


Subsequently in 1965–1970 the method was used to synthesise α-diazo-β-oxosulphones[22–25] and 4-benzenesulphonyl-1,3-dioxo-2,4-bisdiazoalkanes[26]. In particular, the interesting synthesis of 2-diazo-2,3-dihydrothionaphthen-3-one 1,1-dioxide (X) has been achieved by this reaction[22]:

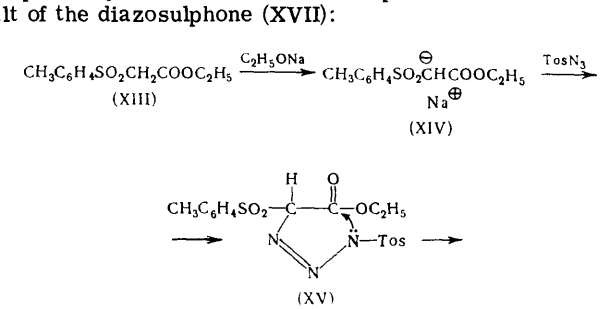


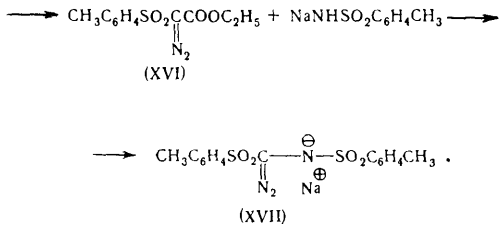
In the first stage 2,3-dihydrothianaphthen-3-one 1,1-dioxide (VI) is converted under the influence of tosyl azide in an alkaline medium into a dipotassium salt of the azo-compound (VII). On being acidified, compound (VII) is converted into the hydrazone (VIII), which is further converted on being refluxed in ethylene glycol into the diazosulphone (X) via the intermediate (IX). The diazosulphone can be converted into the dipotassium salt (VII) on treatment with alkali and the initial compound (VI). Triethylamine[24] or potassium ethoxide[27] can be used as bases and acetonitrile as the solvent[26].

The bis(ethylphenylanilide) of diazomethionic acid (XI)[21] and 9-diazothioxanthene *SS*-dioxide (XII)[27] have been synthesised by this method:



Depending on the solvent and the base, the reaction of tosyl azide with ethyl toluene-*p*-sulphonylacetate (XIII) proceeds in two ways. When equimolecular amounts of sodium ethoxide and tosyl azide are used in an absolute ethanol–ether mixture at 0°C, the sodium salt of *N*-(toluene-*p*-sulphonyl)toluene-*p*-sulphonyldiazoacetamide (XVII) is formed almost immediately. The authors believe that the carbanion (XIV), formed initially from the sulphone (XIII) under the influence of the base, reacts with tosyl azide to form the intermediate adduct (XV). Its decomposition leads to the formation of ethyl toluene-*p*-sulphonyldiazoacetate (XVI) and the sodium salt of toluene-*p*-sulphonamide. The interaction of these two compounds yields the final reaction product—the sodium salt of the diazosulphone (XVII):





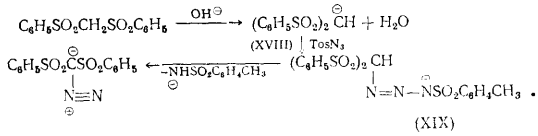
(XVI)

(XVII)

The intermediate diazosulphone (XVI) can be isolated when equimolecular amounts of tosyl azide and the sulphone (XIII) interact in methylene chloride in the presence of triethylamine[25]. The possibility of isolating the diazosulphone (XVI) can be accounted for in this case by the weak solvation of the reaction products by solvent molecules.

The method for the introduction of the diazo-group into bis(arenesulphonyl)methanes with the aid of tosyl azide has been modified recently[28]. The authors suggested that an alkaline aqueous alcoholic solution of the initial bis-(arenesulphonyl)methane be added to a threefold excess of tosyl azide in alcohol. This enables one to obtain stable yields of diazosulphones, while the initial procedure makes it possible to isolate the hydrazones of bis(arenesulphonyl)-formaldehyde in a low yield and only insignificant amounts of bis(arenesulphonyl)diazomethanes.

The reaction involves the formation of the carbanion (XVIII) and the product (XIX) resulting from its coupling with tosyl azide as well as the cleavage of the latter into bis(arenesulphonyl)diazomethane and the toluene-*p*-sulphonamide anion. In particular, bis(mesitylenesulphonyl)-diazomethane has been synthesised by this method:



(XIX)

In view of the critical comments by Heyes and Holt[28] concerning the method for the reduction of the diazo-group into bis(arenesulphonyl)methanes proposed by Klages and Bott[21], we analysed the above investigations and concluded that the method of Heyes and Holt is more effective, since it makes it possible to obtain α-diazo-β-disulphones in high yields and is less laborious.

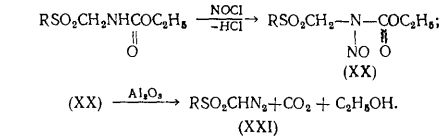
4. Cleavage of *N*-Nitrosourethanes

The alkaline cleavage of *N*-nitrosourethanes is widely used for the synthesis of diazoalkanes and α-diazoketones. This method of synthesis has been most thoroughly developed also in relation to diazosulphones. It is sufficient to point out that the vast majority of alkyl- and aryl-α-diazosulphones[29] and also certain α-alkyl-α-sulphonyldiazomethanes[16] and β-sulphonyldiazo-compounds[30] have been synthesised by this procedure.

The synthesis consists of two stages.

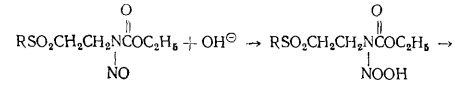
(1) Nitrosation of the initial urethane. Nitrosyl chloride is used as the nitrosating agent. The synthesis of the initial *N*-arenesulphonyl- and *N*-alkanesulphonyl-methylurethanes has been thoroughly worked out[31,32] and does not present much difficulty.

(2) The cleavage of *N*-nitrosourethane to diazosulphone by alumina. The reaction is carried out on a chromatographic column:



(XXI)

The cleavage of *N*-nitrosourethanes with alkali is preferable for the synthesis of certain β-diazosulphones[30]. The reaction can be described schematically as follows:



5. The Cleavage of α-Diazo-β-Oxosulphones

The method reduces to the cleavage of α-diazo-β-oxosulphones with triethylamine in dry methanol[24]:

$$RSO_2CN_2COR^1 \xrightarrow{(C_2H_5)_3N} RSO_2CHN_2 + R^1COOH.$$

The resulting diazosulphone is isolated in the form of triphenylphosphazine:

$$RSO_2CHN_2 + P(C_6H_5)_3 \rightarrow RSO_2CHN{-}NP(C_6H_5)_3 .$$

It is noteworthy that the cleavage reaction is undergone only by α-diazo-β-oxosulphones in which there is an electron-donating substituent (OCH_3, CH_3) in the *para*- and *ortho*-positions of the aryl residue relative to the sulphonyl group. The cleavage of α-acetyl- and α-benzoyl-(*p*-nitrobenzenesulphonyl)diazomethane by triethylamine in methanol leads to products of unknown structure. The cleavage of the above α-diazo-β-oxosulphones to *p*-nitrobenzenesulphonyldiazomethane proceeds without difficulty on alumina in a chloroform–ethanol mixture.

The synthesis of α-diazosulphones by the above method is of limited applicability owing to the low yields of the final products (30–45%) and the difficulties associated with their isolation from the reaction mixture.

III. GENERAL CHARACTERISTICS, STRUCTURE, AND SPECTRA

1. The Characteristics of Diazosulphones

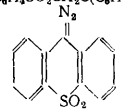
Diazosulphones are bright-yellow substances, the majority of which crystallise readily. Derivatives of monosulphonyldiazomethane[29] and also α-diazo-β-oxosulphones[22–24] can be stored for a long time in the dark at −20°C. Their stability varies widely and is approximately proportional to their melting points. Liquid benzenesulphonyldiazomethane decomposes in the course of several days. The introduction of alkyl substituents in the *p*-position of the benzene ring reduces the stability of α-diazosulphones and they decompose completely in the course of several hours at room temperature. The stability of these compounds increases in ethereal solutions. Crystalline aryl-substituted α-diazosulphones are more stable, although they too decompose slowly at room temperature and in the light. Certain α-diazosulphones (for example phenylmethanesulphonyldiazomethane) show no change in the melting point on storage in the dark in

the course of four months. Derivatives of bis(alkanesulphonyl)- or bis(arenesulphonyl)-diazomethanes are even more stable[21]. They can be stored for a long time in the light at room temperature.

On the other hand, β-diazosulphones are extremely unstable and can exist only in solution[30]. However, their stability increases after the introduction of a phenyl substituent at the α-carbon atom. Thus, as in the case of α-diazoketones, the accumulation of electron-accepting substituents in the diazosulphone molecule and their greater proximity to the diazo-group stabilise the diazo-derivative and increase its thermal and photolytic stabilities.

Derivatives of monosulphonyldiazomethane, α-diazo-β-oxosulphones, and bis(alkanesulphonyl)- and bis-(arenesulphonyl)-diazomethanes are soluble in ether, dichloromethane, and other organic solvents. Potassium diazomethionate is readily soluble in water and slightly in dimethyl sulphoxide. In contrast to diazoalkanes and many α-diazoketones, diazosulphones have no odour. The toxicity of diazosulphones has not been investigated. It has only been noted that these compounds possess no dangerous properties[29]. We believe that it is desirable to investigate the physiological activity of diazosulphones, particularly their carcinogenic and antitumour activities, since these have been shown by other aliphatic diazo-compounds.

Table 1. Parameters of the infrared and ^{1}H NMR spectra of certain diazosulphones.

Diazosulphone	i.r.spectrum $\nu(N_2)$, cm^{-1}	Chemical shift of α-proton τ, p.p.m.	References
$CH_3OC_6H_4SO_2CHN_2$	2101	4.76	29
$NO_2C_6H_4SO_2CHN_2$	2108	4.57	29
$C_6H_5SO_2CHN_2$	2104	4.61	29
$(CH_3)_3CSO_2CHN_2$	2106	4.90	29
$(C_6H_5SO_2)_2CN_2$	2130	—	21
$CH_3C_6H_4SO_2CN_2COCH_3$	2110	—	24
$CH_3C_6H_4SO_2CN_2COOC_2H_5$	2137	—	25
$CH_3C_6H_4SO_2CH_2C(C_6H_5)N_2$	2050	—	30
	2075	—	27
$NO_2C_6H_4SO_2CN_2COCH_3$	2115	—	24

2. Structure and Spectra

Infrared and NMR spectroscopic data[29] (Table 1) reveal a similarity between the structures of the diazo-groups of α-diazosulphones and α-diazoketones. The diazo-group of α-diazosulphones absorbs in the infrared in the region of 2115 ± 15 cm^{-1} and the absorption does not in fact differ from that of α-diazoketones, but is displaced towards higher wavenumbers compared with diazoalkanes. This indicates an increase of the multiplicity of the bond between the nitrogen atoms in the diazo-group of α-diazosulphones compared with diazoalkanes, i.e. the contribution of structure (XXII) to the resonance hybrid is greater than that of structure (XXIII).

$$\underset{\text{(XXII)}}{RSO_2\overset{\ominus}{C}H-\overset{\oplus}{N}\equiv N} \longleftrightarrow \underset{\text{(XXIII)}}{RSO_2CH=\overset{\oplus}{N}=\overset{\ominus}{N}}.$$

The sulphonyl group in α-diazosulphones is responsible for absorption in the region of 1330 and 1140 cm^{-1} in the infrared spectra. In the NMR spectra of α-diazosulphones[29] (Table 1) the CHN_2 proton gives rise to a signal between τ = 4.57 and 4.98. The α-proton in α-diazoacetone gives rise to τ = 4.82. In the series of aryl-substituted α-diazosulphones *para*-substituents have some influence on the position of the absorption band of the diazo-group in the infrared spectra and on the α-proton chemical shift. Electron-donating substituents, for example the methoxy-group, promote an increase of electron density at the α-carbon atom. This is indicated by infrared and NMR spectroscopic data. Thus the absorption of the diazo-group in the infrared spectra of *p*-methoxybenzenesulphonyldiazomethane and *p*-nitrobenzenesulphonyldiazomethane is at 2103.3 and 2108.2 cm^{-1} respectively and the α-proton signals in the NMR spectra have τ = 4.75 and 4.57 respectively. Naturally an increase of electron density of the α-carbon atom of the diazosulphone leads to enhanced shielding of the α-proton and hence to higher chemical shifts.

Owing to the magnetic anisotropy of the benzene ring, the chemical shifts of the α-protons of aryl-substituted α-diazosulphones are smaller than for the alkyl-substituted derivatives[29].

The introduction of a second arenesulphonyl group into the α-diazosulphone molecule tends to increase the contribution of structure (XXII) to the resonance hybrid of the α-diazosulphone, as shown, for example, by the shift of the absorption band of the diazo-group in the infrared spectrum towards higher wavenumbers by 20–30 cm^{-1}. Thus the diazo-group in bis(benzenesulphonyl)diazomethane[21] absorbs in the region of 2130 cm^{-1}, while that in benzenesulphonyldiazomethane absorbs in the region of 2104 cm^{-1}. The substitution of the α-hydrogen atom in diazosulphones by an acyl or alkoxycarbonyl residue also tends to shift the infrared absorption band of the diazo-group towards higher wavenumbers. This is illustrated by α-acetyl-α-(*p*-nitrobenzenesulphonyl)diazomethane[24], *p*-nitrobenzenesulphonyldiazomethane[29], and ethyl toluene-*p*-sulphonyldiazoacetate[25] (Table 1).

Table 2. Parameters of the ultraviolet spectra of certain α-diazosulphones* *m*-$XC_6H_4SO_2CHN_2$.

X	ν_{max}, nm	lgε	X	ν_{max}, nm	lgε
CH_3O	390	1.87	CF_3	383	1.84
CH_3	390	1.79	NO_2	385	1.97
Cl	385	1.84			

*The spectra were recorded in solution in 40% dioxan–water.

The introduction of the methylene group into α-diazosulphones leads to the breakdown of conjugation between the diazo- and sulphonyl groups, i.e. to a decrease of the contribution of structure (XXII) to the resonance hybrid. All these factors are clearly reflected in the infrared spectra of β-diazosulphones, where the absorption of the diazo-group is displaced towards lower wavenumbers by 30–50 cm^{-1} compared with α-diazosulphones. For example, 1-phenyl-2-(toluene-*p*-sulphonyl)diazomethane[30] and 9-diazothioxanthene SS-dioxide[21] absorb in the region of 2050 and 2075 cm^{-1} respectively.

The ultraviolet spectra of α-diazosulphones have not been investigated in detail[33–35]. Those of *m*-substituted aryldiazosulphones, whose parameters are presented in

Table 2, [34] show that diazosulphones absorb in the region of 390 nm, which corresponds to the $n \rightarrow \pi^*$ transition in the diazo-group.

Table 3. The influence of the solvent on the frequency of the $n \rightarrow \pi^*$ transition in the ultraviolet spectra of $RSO_2.CHN_2$.

R	Solvent	ν_{max}, cm^{-1}	$\lg \varepsilon_{max}$
m-$CH_3C_6H_4$	CCl_4	25000	1.88
	C_2H_5OH	25300	1.84
	40% dioxan-H_2O	25600	1.79
m-$CH_3OC_6H_4$	CCl_4	24700	1.88
	C_2H_5OH	25200	1.86
	40% dioxan-H_2O	25600	1.87
$(CH_3)_3C$	CCl_4	25600	1.21
	C_2H_5OH	25800	1.23
	40% dioxan-H_2O	26300	1.26

The polarity of the solvent influences the energy of the $n-\pi^*$ transition, which is reflected in the position of the absorption maximum of the diazo-group. Table 3 shows that more polar solvents shift the absorption maximum of α-diazosulphones towards shorter wavelengths.

Like α-diazoketones, α-diazosulphones form hydrogen bonds[35,36]. In both cases the methine hydrogen of the diazo-fragment serves as the proton donor and the acceptor is the sulphonyl or carbonyl group. α-Diazosulphones are more powerful proton donors and weaker proton acceptors than α-diazoketones.

IV. CHEMICAL PROPERTIES

Three types of reactions are characteristic of diazosulphones: (1) reactions with evolution of nitrogen; (2) reactions involving the nitrogen of the diazo-group; (3) substitution of the α-hydrogen atom.

Reactions of the first type have been most completely investigated and those of the second and particularly of the third type much less so. In discussing the chemical properties of diazosulphones, one must bear in mind that these compounds have been studied for only 10–15 years and therefore many interesting reactions of this class of compounds have still not been investigated.

The chemical reactions of diazosulphones known at present are summarised below in relation to different types of reaction mechanisms.

1. Reactions Involving the Formation of Carbonium Ions

Reactions of this series include those of diazosulphones with water, acids, t-butyl hypochloride, sulphuryl chloride, and nitrogen oxides.

The study of the hydrolysis of α-diazosulphones[34,37-40] in water and water–dioxan mixtures showed that the acid-catalysed decomposition proceeds via the bimolecular *A*-2 mechanism. The initial diazosulphone is reversibly protonated in the first stage, while in the second, rate-determining stage the resulting diazonium ion interacts with a molecule of the nucleophilic agent to form the final reaction product:

$$RSO_2CHN_2 \overset{H^\oplus}{\rightleftharpoons} RSO_2CH_2N_2^\oplus$$

$$RSO_2CH_2N_2^\oplus + \text{nucleophilic agent} \xrightarrow{\text{slow}} \text{product} + N_2 .$$

Studies in recent years established[41] that the hydrolysis of 4-methylbenzenesulphonyldiazomethane in a water–dioxan mixture in the presence of perchloric acid involves the protonation of the oxygen of the sulphonyl group and the *A*-1 mechanism, and the *A*-2 mechanism in the presence of hydrochloric acid in view of the more marked nucleophilic properties of chloride ions.

Electron-accepting substituents diminish and electron-donating substituents increase the rate of hydrolysis of aryl-substituted α-diazosulphones[34]. Similar observations had been made previously in the series of α-diazoketones[42] and aryldiazomethanes[43].

It is noteworthy that the hydrolysis of α-methyl-α-(toluene-*p*-sulphonyl)diazomethane[16] in a water–dioxan mixture under the influence of perchloric acid takes place differently and, depending on the reaction time, gives rise to different products. After 30 min, the reaction mixture contains toluene-*p*-sulphinic acid, acetaldehyde, and toluene-*p*-sulphonylethylene, and after 36 h acetaldehyde and 1,2-di(toluene-*p*-sulphonyl)ethane. The latter is formed as a result of the reaction of toluene-*p*-sulphonylethylene with the toluene-*p*-sulphinic acid present in the reaction mixture.

The decomposition of potassium diazomethionate[44] in aqueous solutions is catalysed by strong inorganic acids. However, the reaction begins only at a fairly high acid concentration. The hydrolysis is particularly rapid in the presence of sulphuric and perchloric acids. The addition of chloride ions reduces appreciably the reaction rate. The mechanism of the decomposition of potassium diazomethionate has not been described. Presumably in the first stage of the reaction the stronger acid displaces diazomethionic acid from its salt and the former is then cleaved.

In inert solvents α-diazosulphones form with inorganic and organic acids the esters of the corresponding α-hydroxymethyl sulphones. Certain differences between the reactivities of mono- and di-substituted α-diazosulphones and α-diazo-β-oxosulphones have been noted.

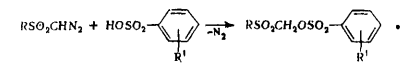
The reactions of monosubstituted α-diazosulphones with 70% perchloric acid[45,46] in methylene chloride give rise to the formation of the covalent perchlorates (XXIV) in 45% yield and α-hydroxymethyl sulphones (XXV) in 10% yield:

$$RSO_2CHN_2 + HClO_4 \begin{cases} \xrightarrow{CH_2Cl_2} RSO_2CH_2N_2^\oplus \cdot ClO_4^\ominus \rightarrow RSO_2CH_2OClO_3 \\ \qquad\qquad (XXVI) \qquad\qquad (XXIV) \\ \xrightarrow[CH_2Cl_2]{H_2O} RSO_2CH_2OH \\ \qquad\qquad (XXV) \end{cases}$$

In acetonitrile or propionitrile the yield of the perchlorate (XXIV) is lower and sulphonylmethylamides of acetic and propionic acids ($RSO_2CH_2NHCOAlk$; Alk = CH_3 or C_2H_5) are formed. The authors believe that the ion pair (XXVI), formed as a result of attack by perchloric acid, is readily converted into the perchlorate (XXIV) owing to the low polarity of the solvent. The hydroxy-derivative (XXV) is formed as a result of competition between water and perchloric ions in attacking the diazonium ion. When the ion pair (XXVI) is attacked by the alkyl cyanide, which is facilitated by the solvation of (XXVI) by the polar solvent molecules, and the resulting intermediate adduct (XXVII) is hydrolysed, sulphonylmethylamides are formed:

$$(XXVI) + R^1CN \rightarrow \underset{(XXVII)}{RSO_2CH_2\overset{\oplus}{N}CR^1ClO_4^\ominus} \rightarrow RSO_2CH_2NHCOR^1 + HClO_4 .$$

On interaction with α-diazosulphones, aromatic sulphonic acids give rise to sulphonates derived from α-hydroxymethyl sulphones[45,47]:



The trifluoromethanesulphonates derived from α-hydroxymethyl sulphones, which are readily formed when α-diazosulphones react with trifluoromethanesulphonic acid, are of considerable interest[48]:

$$CH_3C_6H_4SO_2CHN_2 + HSO_3CF_3 \rightarrow CH_3C_6H_4SO_2CH_2OSO_2CF_3 + N_2 .$$

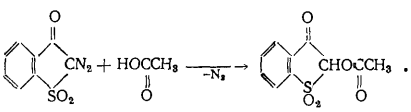
These compounds react readily with various nucleophilic agents via an S_N2 mechanism with formation of α-substituted sulphones. α-Diazosulphones react without difficulty with nitric and hydrochloric acids[29,49], forming derivatives of these acids:

$$RSO_2CHN_2 + HX \rightarrow RSO_2CH_2X + N_2 ;$$
$$X = Cl^{\ominus},\ ONO_2^{\ominus} .$$

The reaction of di(benzenesulphonyl)diazomethane with hydriodic acid[50] results in the formation of di(benzenesulphonyl)methane instead of the expected di(benzenesulphonyl)iodomethane. Evidently the intermediate di(benzenesulphonyl)iodomethane is reduced by a second molecule of hydriodic acid to di(benzenesulphonyl)methane:

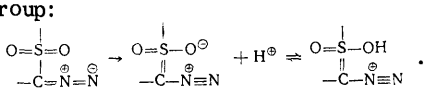
$$(C_6H_5SO_2)_2CN_2 \xrightarrow[-N_2]{HI} [(C_6H_5SO_2)_2CHI] \xrightarrow[-I_2]{HI} (C_6H_5SO_2)_2CH_2 .$$

α-Diazo-β-oxosulphones are less reactive with respect to acids than α-diazosulphones. Thus 2-diazo-2,3-dihydrothianaphthen-3-one 1,1-dioxide reacts with acetic acid only on heating and in the presence of copper as the catalyst[22]:



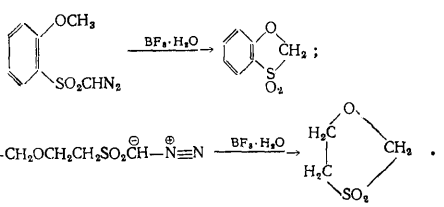
Bis(arenesulphonyl)diazomethanes are even more resistant to acids. For example, bis(benzenesulphonyl)-diazomethane[19] can be recrystallised from glacial acetic acid.

This behaviour of α-diazo-β-oxosulphones and bis-(arenesulphonyl)diazomethanes can be accounted for by the capture of the proton attacking the α-carbon atom by the sulphonyl group:

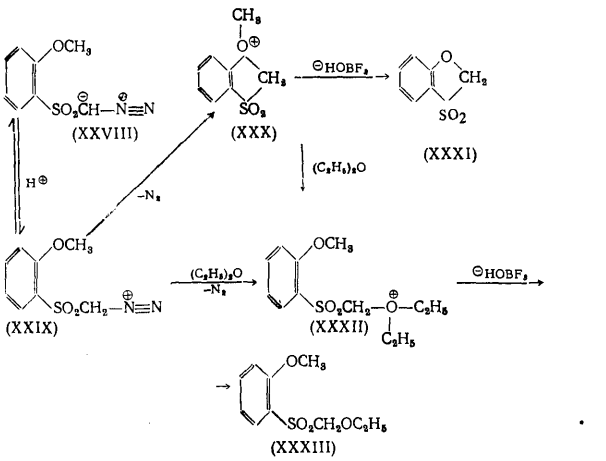


Similar observations were made also in the series of α-diazoketones. However, owing to the greater reactivity of the sulphonyl group, these phenomena are more pronounced in the case of α-diazosulphones.

Under the influence of acids, some α-diazosulphones cyclise. Thus *o*-methoxybenzenesulphonyldiazomethane and the benzyl ether of hydroxyethanesulphonyldiazomethane in ethereal solutions are converted under the influence of hydrated boron trifluoride into 1,3-benzoxathiolan 3,3-dioxide and 1,3-oxathiolan 3,3-dioxide respectively[51]:



In the first reaction stage the initial diazosulphone (XXVIII) is protonated and the resulting diazonium ion (XXIX) splits off nitrogen, being converted into the oxonium ion (XXX). The latter is converted into the final product—1,3-benzoxathiolan 3,3-dioxide. When (XXIX) or (XXX) reacts with the solvent, the intermediate oxonium ion (XXXII) is formed and then converted into α-ethoxy-α-(*o*-methoxybenzenesulphonyl)methane (XXXIII):



When ethyl ether is excluded from the reaction mixture and the reaction is carried out in methylene chloride, the yield of the oxathiolan (XXXI) increases to 72% compared with 65%.

Potassium diazomethionate reacts with hydrogen halides to form salts of halogenomethionic acids[9,52]:

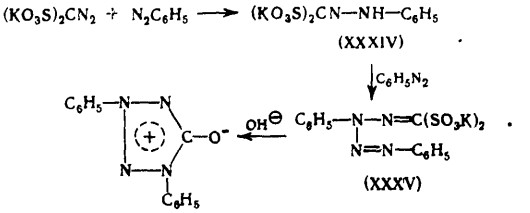
$$(KO_3S)_2CN_2 + HHal \xrightarrow{Hal=I,Br} (KO_3S)_2CHHal + N_2 .$$

When potassium diazomethionate was allowed to react with iodine[9], the potassium salt of diiodomethanedisulphonic acid was isolated:

$$(KO_3S)_2CN_2 + I_2 \rightarrow (KO_3S)_2CI_2 + N_2 .$$

It is noteworthy that the relatively little investigated methionic acid derivatives formed in these reactions are of significant interest as chemical reagents.

Potassium diazomethionate reacts with aromatic diazo-compounds. Thus the reaction with benzenediazonium acetate gives rise to the phenylhydrazone (XXIV)[53] which is converted in the presence of an excess of benzenediazohydroxide into potassium diazobenzenephenylhydrazonomethanedisulphonate (XXXV). The latter is converted under the influence of alkali into 1,3-diphenyltetrazolone[54]:



Sodium diazomethionate readily reacts with sodium bisulphite to form the salt of methanetrisulphonic acid[9,17]:

$$(NaO_3S)_2CN_2 + NaHSO_3 \rightarrow (NaO_3S)_2CHSO_3Na .$$

The interaction of α-diazosulphones with t-butyl hypochlorite proceeds via an ionic mechanism. Various products may be obtained, depending on the solvent[55]:

$$RSO_2CHN_2 + (CH_3)_3COCl \begin{cases} \xrightarrow[\text{or } CH_2Cl_2]{(CH_3)_3COH} RSO_2CH(Cl)OC(CH_3)_3 + N_2 \\ \text{(XXXVII)} \\ \xrightarrow{C_2H_5OH} RSO_2CH(Cl)OC_2H_5 + N_2 \\ \text{(XXXVIII)} \end{cases}$$

The first stage of this interesting reaction involves the addition of the electrophilic chlorine of t-butyl hypochlorite to the α-carbon atom of the diazosulphone with formation of the ion pair $RSO_2CH(Cl)N_2^+.BtO^-$ (XXXVI) solvated by t-butyl alcohol. The sulphone (XXXVII) is formed as a result of the displacement of nitrogen either by the t-butoxide anion or by t-butyl alcohol. In ethanol the sulphone (XXXVIII) is produced as a result of the solvolysis of the ion pair (XXXVI). It is noteworthy that the decomposition of (XXXVI) is accompanied by the formation of several side products, the composition of which has not so far been established.

In contrast to α-diazosulphones, α-diazoketones react with t-butyl hypochlorite to form acetals[55]:

$$RCOCHN_2 + (CH_3)_3COCl \xrightarrow{C_2H_5OH} RCOCH\begin{matrix}OC_2H_5\\OC_2H_5\end{matrix}.$$

This can be accounted for by the different capacities of the chlorine atom in α-alkoxy-α-chloromethylsulphones (XXXVII) or (XXXVIII) and α-alkoxy-α-chloromethylketones (XXXIX) for nucleophilic substitution[56]:

$$RCOCH(Cl)OC_2H_5 + C_2H_5OH \xrightarrow[-HCl]{} RCOCH(OC_2H_5)_2,$$

$$RSO_2CH(Cl)OC_2H_5 + C_2H_5OH \not\rightarrow RSO_2CH(OC_2H_5)_2.$$

The driving force of the reaction of α-diazosulphones with sulphuryl chloride in ether[57] is attack on the diazo-derivative by the chloronium cation formed when sulphuryl chloride reacts with ether. The resulting diazonium ion (XL) is converted in ether into the oxonium ion (XLI). As a result of nucleophilic attack by the chloride ion, the latter is converted into α-alkoxy-α-chloro-sulphone:

$$SO_2Cl_2 + ROR \rightarrow SO_2 + Cl^{\oplus} + Cl^{\ominus} + ROR;$$

$$R^1SO_2CHN_2 + Cl^{\oplus} \rightarrow \underset{\text{(XL)}}{R^1SO_2CHClN_2^{\oplus}};$$

$$(XL) + ROR \xrightarrow[-N_2]{} R^1SO_2CHCl\overset{\oplus}{O}R_2;$$

$$(XLI) + Cl^{\ominus} \rightarrow R^1SO_2CHClOR + RCl.$$

It is noteworthy that there has recently been a growth of interest in reactions of diazo-derivatives with compounds which behave as donors of positive halogenonium ions. Many of these reactions make possible new methods for the synthesis of acetals and halogeno-derivatives of ethers, sulphones, heterochain compounds, and heterocyclic compounds. As an example, one may quote the reactions of diazomethane and diazoacetic ester with bromotrinitromethane[58], which lead respectively to 3-nitroisoxazoline *N*-oxide and ethyl α-bromo-ββ-trinitropropionate:

$$BrC(NO_2)_3 \begin{cases} \xrightarrow{CH_2N_2} H_2C\begin{matrix}C(NO_2)_2\\ \\ N^{\oplus}-O^{\ominus}\\ O\end{matrix}\!\!\!

of silver oxide and leads to the formation of *p*-methoxyphenyl methoxymethyl sulphone:

$$CH_3OC_6H_4SO_2CHN_2 \xrightarrow[-N_2]{h\nu,\ CH_3OH,\ Ag_2O} CH_3OC_6H_4SO_2CH_2OCH_3 .$$

The formation of a sulphonylcarbene is also observed in the thermal decomposition of benzenesulphonyldiazomethane in benzene[65]. Together with a carbene dimerisation product—1,2-di(benzenesulphonyl)ethylene, a small amount of the product resulting from the insertion of the carbene in the C–H bond of benzene—benzenesulphonylphenylmethane—is formed[65]. Apart from these products, the ester of benzenesulphonic acid and benzenesulphonylmethanol (XLIX) is produced. The authors believe that its formation can be accounted for by the decomposition of the initial diazosulphone into the benzenesulphonyl radical $RSO_2^{\cdot}$, which captures oxygen. The resulting sulphonyl oxide radical $RSO_2^{\cdot}$ reacts with the benzenesulphonylmethyl radical formed by the reaction

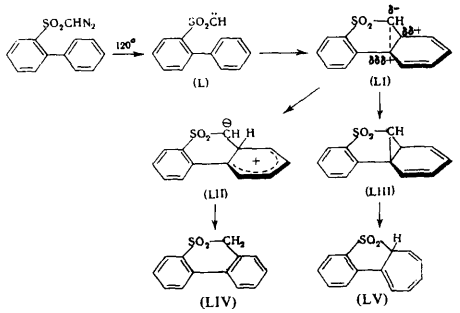
$$C_6H_5SO_2CH: + RH \rightarrow C_6H_5SO_2CH_2\cdot + R\cdot$$

The dimerisation of the above radicals gives rise to the final ester (XLIX). Compound (XLVII) is not in fact formed in the photolysis of (XLVI) in benzene, the yield of (XLVIII) remains the same, and the yield of (XLIX) increases appreciably:

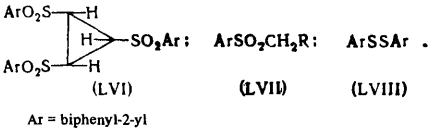
$$C_6H_5SO_2CHN_2\ (XLVI) \xrightarrow{C_6H_5SO_2CHN_2} C_6H_5SO_2CH{=}CHSO_2C_6H_5\ (XLVII)$$
$$C_6H_5SO_2CHN_2\ (XLVI) \xrightarrow{C_6H_6} C_6H_5SO_2CH_2C_6H_5\ (XLVIII)$$
$$C_6H_5SO_2CHN_2\ (XLVI) \rightarrow C_6H_5SO_2CH_2OSO_2C_6H_5\ (XLIX)$$

The photolysis and thermolysis of compound (XLVI) in cyclohexene[65] lead to an *exo*- and *endo*-7-benzenesulphonylnorcaranes in proportions of 68 : 32; compounds (XLVII) and (XLIX) were not detected. The thermal decomposition of benzenesulphonyldiazomethane in cyclohexane leads to the formation of the insertion product $C_6H_{11}CH_2SO_2C_6H_5$ in 43% yield and of compound (XLIX) in 6.9% yield. The photolysis of the diazosulphone (XLVI) in the same solvent gives rise to the same insertion product in 12% yield and to compound (XLIX) in 39% yield.

The thermal decomposition of biphenyl-2-sulphonyldiazomethane at 120°C leads to intramolecular products resulting from the insertion of a carbene (L) in a C–H or C–C bond[66]. According to the authors, this reaction proceeds via an intermediate intramolecular complex (LI), which is converted into the σ-complex (LII) or into the intermediate norcaradiene (LIII). The latter is converted into the product resulting from insertion in a C–H bond [compound (LIV)] or a C–C bond [compound (LV)]:



Apart from the two cyclic sulphones (LIV) and (LV), the authors detected the cyclopropane derivative (LVI), the sulphone (LVII), and the disulphide (LVIII):



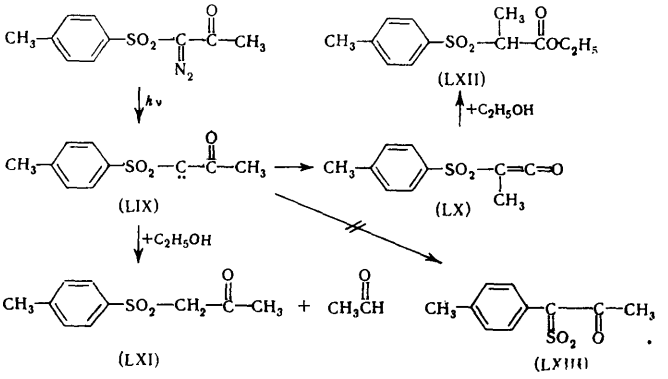
Ar = biphenyl-2-yl

The formation of compound (LVIII) can be explained by the decomposition of the initial diazosulphone into aryl-substituted sulphonyl groups with subsequent reduction and dimerisation. The sulphone (LVII) is produced as a result of the insertion of the sulphonylcarbene in a C–H bond of the solvent and the cyclopropane (LVI) is normally formed as a result of the trimerisation of an arenesulphonylcarbene.

The formation of sulphonylcarbenes on ultraviolet irradiation of di(benzenesulphonyl)diazomethane in polar solvents made it possible to develop an interesting method for the synthesis of ylids[19]:

$$(C_6H_5SO_2)_2CN_2 \xrightarrow[-N_2]{} (C_6H_5SO_2)_2C: \xrightarrow{(CH_3)_2SO} (CH_3)_2\overset{\oplus}{S}-\overset{\ominus}{C}(SO_2C_6H_5)_2 .$$

Attempts to carry out the Wolff rearrangement for compounds in the series of α-diazo-β-oxosulphones during their photolytic or thermal decomposition have been described. However, the study of the photolysis of α-acetyl(toluene-*p*-sulphonyl)diazomethane[67] in ethanol showed that the carbene (LIX) formed after the elimination of nitrogen rearranges either into the keten (LX) (an α-ketocarbene-like behaviour) or reacts with ethanol, being converted into acetyl(toluene-*p*-sulphonyl)methane (LXI) and acetaldehyde. On interaction with ethanol, methyl(toluene-*p*-sulphonyl)keten (LX) gives rise to ethyl α-(toluene-*p*-sulphonyl)propionate (LXII):

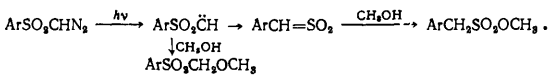


The product of the addition of ethanol to acetyl tolyl sulphene (LXIII) was not isolated. This is evidence that the rearrangement of the carbene (LIX) into the sulphene (LXIII), resembling the Wolff rearrangement, does not occur in this case.

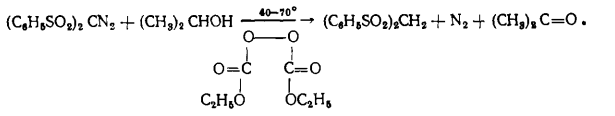
The thermolysis of α-benzoylbenzenesulphonyldiazomethane at 100–110°C in mesitylene[25] leads to formation of phenylbenzenesulphonylketen (LXIV), which is converted in the presence of amines into *N*-substituted phenylbenzenesulphonylacetamides:

$$C_6H_5SO_2CN_2COC_6H_5 \rightarrow \underset{C_6H_5SO_2}{\overset{C_6H_5}{>}}C{=}C{=}O\ (LXIV) \xrightarrow{H_2NR} \underset{C_6H_5SO_2}{\overset{C_6H_5}{>}}CH-C(=O)NHR .$$

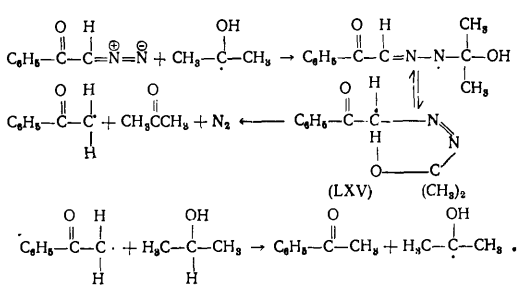
When aryl-substituted α-diazosulphones were irradiated in methanol at −10°C in an atmosphere of nitrogen[67], the methyl ether of arenesulphonylmethanol and (in a low yield) the methyl ester of α-arylmethanesulphonic acid were isolated. The last compound is probably formed as a result of the Wolff rearrangement of the arenesulphonylcarbene into an aryl sulphene, which then interacts with methanol:



When di(benzenesulphonyl)diazomethane is heated with isopropyl alcohol in the presence of diethyl peroxydicarbonate, the products are radicals which react with the above diazosulphone to form the product of the reductive elimination of nitrogen[69]:

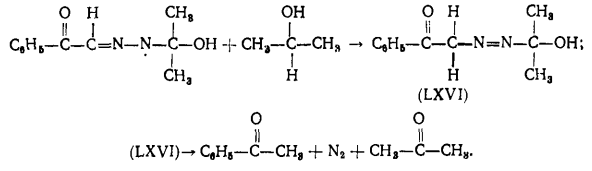


The reaction with α-diazoketones proceeds similarly. The following mechanism has been proposed:



The decomposition of diethyl peroxydicarbonate results in the elimination of a proton from isopropyl alcohol with formation of the isopropyl radical, which reacts with the diazoketone to form a hydrazonyl radical with an unpaired electron at the nitrogen atom. The latter is in equilibrium with the C-radical form (LXV). The radical (LXV) decomposes into acetone, nitrogen, and a benzoylmethyl radical. The interaction of the last species with the solvent leads to the product of the reductive elimination of nitrogen and the initial isopropyl alcohol.

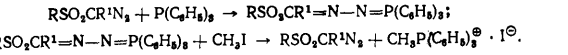
According to an alternative mechanism, the hydrazonyl radical formed in the first stage reacts with the solvent to produce the azo-compound (LXVI), which decomposes with evolution of nitrogen into the final reaction product and acetone:



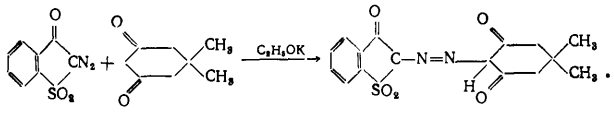
3. Reactions Involving the Nitrogen of the Diazo-Group

An important section of the chemistry of diazosulphones comprises reactions involving the nitrogen of the diazo-group; some of these were studied previously for other diazo-derivatives.

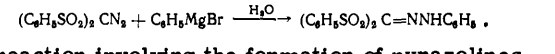
Triphenylphosphine reacts with diazosulphones to form triphenylphosphazines[19,24,27,29,30], which can be used to identify diazosulphones and to obtain them in a pure form:



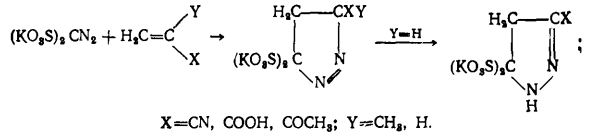
α-Diazo-β-oxosulphones react with compounds containing an activated methylene group to form azo-derivatives[22]:



Diekmann[19] observed the formation of the phenylhydrazone of di(benzenesulphonyl)formaldehyde in the reaction of di(benzenesulphonyl)diazomethane with phenylmagnesium bromide:

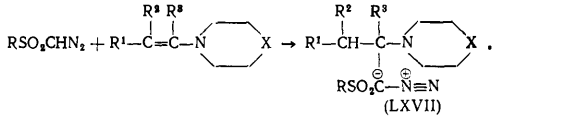


The reaction involving the formation of pyrazolines, which is well known in the series of diazoalkanes[70], has also been described for diazosulphones in relation to the interaction of potassium diazomethionate with a number of unsaturated compounds[71]:

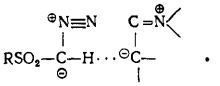


X=CN, COOH, $COCH_3$; Y=CH_3, H.

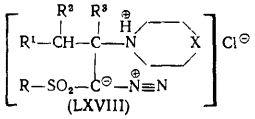
It has recently been observed that α-diazosulphones readily add to the double bonds of substituted enamines[72] with formation of products of the *C*-alkylation of the α-carbon atom of the diazosulphone [compound (LXVII)], but not pyrazolines (as happens with α-diazoketones):



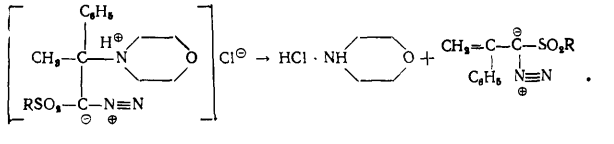
This difference in the behaviour of α-diazosulphones and α-diazoketones was explained by the greater capacity of the methylidyne protons of α-diazosulphones for the formation of hydrogen bonds with enamines in the transition complex:



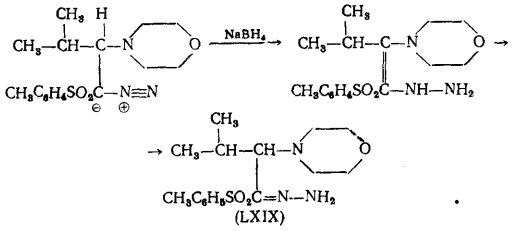
The adduct (LXVII) is stable, forming with hydrochloric acid in ether the hydrochloride (LXVIII), which can undergo further reactions:



Thus, for $R^1 = R^2 = H$, $R^3 = C_6H_5$, and X = O, morpholine hydrochloride is split off in chloroform at room temperature and an unsaturated diazosulphone—3-diazo-2-phenyl-3-(toluene-*p*-sulphonyl)prop-1-ene—is formed:

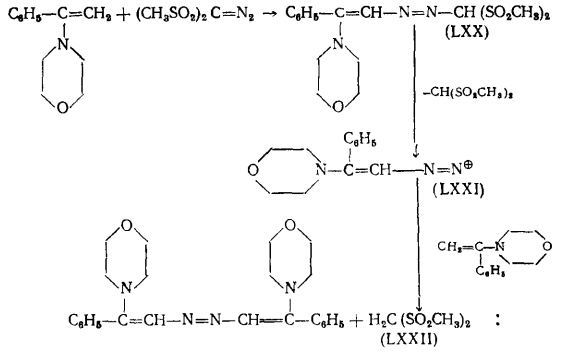


The diazosulphone (LXVII) (R = $CH_3C_6H_4$, $R^1 = R^2 = CH_3$, R^3 = H, and X = O) is reduced with sodium tetrahydroborate in methanol to 1-hydrazino-3-methyl-2-morpholino-1-(toluene-*p*-sulphonyl)but-1-ene, which isomerises to the hydrazone (LXIX) under the influence of hydrochloric acid:



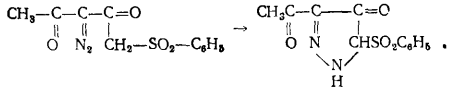
(LXIX)

The reaction of di(alkanesulphonyl)diazomethanes with enamines proceeds via a different mechanism. In the reaction of di(methanesulphonyl)diazomethanes[73] with α-morpholinostyrene the initial product is the azo-compound (LXX), which splits off the anion of di(methanesulphonyl)methane, forming the diazonium ion (LXXI). The latter reacts with a second enamine molecule to form 1,6-dimorpholino-1,6-diphenyl-3,4-diaza-1,3,5-hexatriene and di(methanesulphonyl)methane (LXXII):



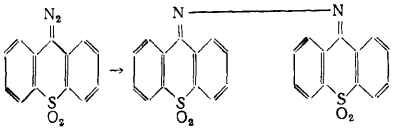
(LXXII)

The interesting intramolecular cyclisation of 3-diazo-5-benzenesulphonylpentane-2,4-dione to the corresponding pyrazolone (LXXIII) under the influence of potassium ethoxide[74] belongs to the class of reactions proceeding without the evolution of nitrogen:

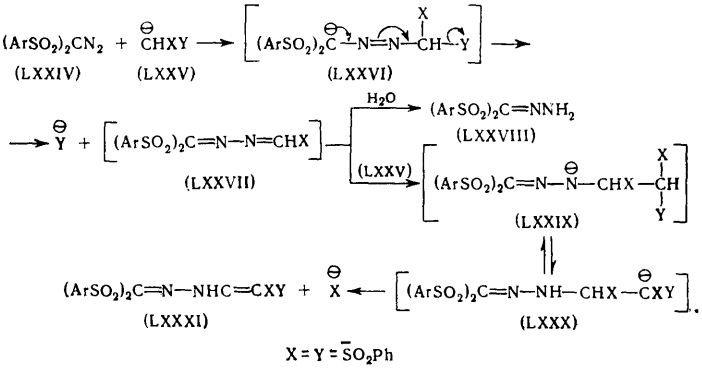


(LXXIII)

Under the same conditions, 9-diazothioxanthene *SS*-dioxide forms the azene derived from 9-oxothioxanthene *SS*-dioxide[27]:



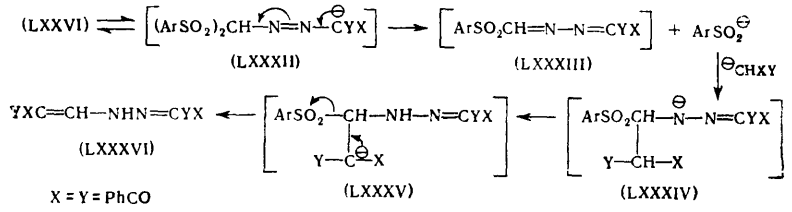
Heyes and Holt[28] described recently an interesting reaction between di(arenesulphonyl)diazomethanes and the sodium salt of di(benzenesulphonyl)methane. It proceeds in tetrahydrofuran at 0°C and leads to the formation of sodium benzenesulphinate and a vinylhydrazone (LXXXI):



X = Y = SO_2Ph

The authors explain the formation of vinylhydrazones by the coupling of the aryldiazosulphone (LXXIV) to the carbanion (LXXV). The coupling of diazosulphones to triphenylphosphine and phenylmagnesium bromide has already been mentioned. According to the authors, this reaction is a first example of reactions where the nucleophilic agent substitutes a hydrogen atom at a carbanionic centre. The elimination of the arenesulphinate ion from the adduct (LXXVI) probably leads to the azine (LXXVII), which hydrolyses to the hydrazone (LXXVIII) in aqueous solvents. In a non-aqueous medium the nucleophilic attack on the azine (LXXVII) by a second carbanionic species leads to the formation of the adduct (LXXIX), whose tautomer (LXXX) can split off a sulphinate ion to form the vinylhydrazone (LXXXI).

If the carbanion contains carbonyl groups, then the adduct (LXXVI) is probably converted into the tautomer (LXXXII). Otherwise it is impossible to explain the splitting off of the sulphinate ion [(LXXXII) → (LXXXIII)]. This view is supported by the finding that the remaining sulphonyl group is split off from the azine (LXXXIII) with subsequent attack by a second carbanionic species, probably in accordance with the scheme (LXXXIII) → (LXXXIV) → (LXXXV) → (LXXXVI). The tetracarbonylvinylhydrazone (LXXXVI) is formed via a mechanism involving the formation of a tetrasulphonylvinylhydrazone:



X = Y = PhCO

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From the time when α-diazosulphones began to be studied on a wide scale, 12 years have elapsed. However, during this brief period the fundamentals of their chemistry have been worked out, their characteristics have been discovered, and practical applications of this interesting class of compounds have been outlined.

The interest in α-diazosulphones is due to various causes. In the first place one should mention that these compounds are valuable preparative reagents, which permit the introduction of the sulphonyl group into various organic compounds. α-Diazosulphones lead to interesting heterocyclic system, such as sulphonylfuroxans[60], oxathiolans[51], etc.[54,71]. They serve as the starting materials for the synthesis of sulphonylcyclopropanes[63,64].

The study of the biological activity of α-diazosulphones is of considerable interest. The stable and relatively non-toxic potassium diazomethionate, which exhibits antitumour activity, is striking in this respect. By analogy with α-diazoketones, α-diazosulphones can evidently exhibit mutagenic and anticonvulsant activity[75].

The presence of the nitrogen atom, which can be split off on heating or under the influence of chemical agents, permits the use of α-diazosulphones, particularly potassium diazomethionate, as agents for the formation of sponge rubber[76].

A number of characteristics of the chemical behaviour of α-diazosulphones have been discovered. Thus, in contrast to α-diazoketones, α-diazosulphones do not as a rule undergo the Wolff rearrangement, add readily to the double bond of enamines with retention of the diazo-group, react in a characteristic manner with t-butyl hypochlorite, etc.

Further elucidation of the differences between the structures and chemical properties of the diazo-group in α-diazosulphones and other aliphatic diazo-compounds will help deepen our knowledge of this field of chemistry.

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